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(54) Title: FUCOSYLATED GLYCOSIDES AS INHIBITORS OF BACTERIAL ADHERENCE

(57) Abstract

Mono-, di-, tri- or oligosaccharide glycoside derivatives having at least one terminal group which is derived from L-fucose. The compounds are useful for therapy or prophylaxis in conditions involving infection by Heliobacter pylori of human gastric mucosa. Another object of the present invention is to provide a process for their preparation and pharmaceutical compositions.

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FUCOSYLATED GLYCOSIDES AS INHIBITORS OF BACTERIAL ADHERENCE

FIELD OF THE INVENTION

The present invention relates to the use of L-fucose-containing glycoside derivatives for the preparation of pharmaceutical compositions for the treatment or prophylaxis of conditions involving gastrointestinal infections by *Helicobacter pylori*, a method of treating such conditions using the derivatives, as well as novel glycoside derivatives.

BACKGROUND OF THE INVENTION

Helicobacter pylori is a microaerophilic spiral shaped organism (originally assigned to the genus *Campylobacter*) which is found in the stomach and generally appears to have an exclusive habitat in the human gastric mucosa. It has been estimated that this bacterium infects the gastric mucosa of more than 60% of adult humans by the time they are 60 years old. Moreover, *H. pylori* has been implicated as a contributing factor in a number of pathological conditions, including acute (type B) gastritis, gastric and duodenal ulcers, atrophic gastritis, and gastric adenocarcinoma.

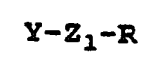
Tissue tropism of bacteria is partly governed by the ability of a bacterial strain to adjust to the local chemical environment in its specific habitat. In addition, adherence is a necessary prerequisite for colonization in order to prevent removal from the new habitat, e.g. through peristalsis in the gastrointestinal tract. In mammals, bacteria adhere to proteins or glycoconjugates (glycosphingolipids, glycoproteins) on or in the vicinity of epithelial cell surfaces (mucus), and a number of specific bacterial adhesin-protein and adhesin-carbohydrate interactions have been described in the literature.

With respect to *H. pylori*, studies in model systems such as mouse adrenal Y-1 cells (see D. G. Evans, D. J., Jr. Evans, and

D. Y. Graham, (1989) *Infect. Immun.* 57, 2272-2278) have suggested that surface-associated fl xible fibrillar structures that surround this bacterium function as adhesins or colonization factor antigens to mediate the binding of *H. pylori* to cellular sialic acid-containing glycoprotein receptors.

SUMMARY OF THE INVENTION

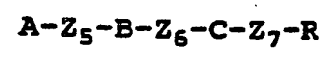
The invention concerns the use of mono-, di-, tri- or oligosaccharide glycoside derivatives having at least one terminal group Y, as defined below, derived from L-fucose, said derivatives being compounds of the general formula Ia, Ib, Ic, Id, Ie or If



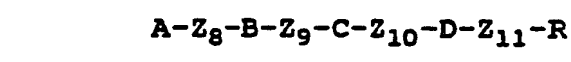
Ia

Ib

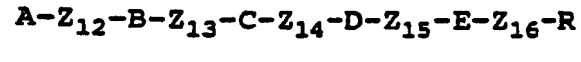
Ic



Id



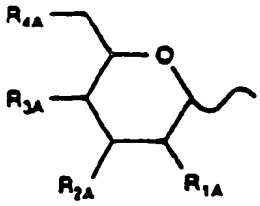
Ie

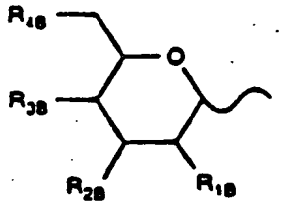
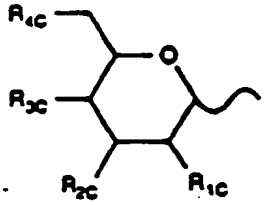


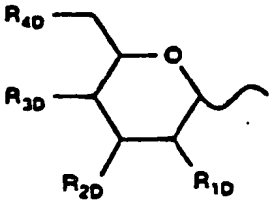
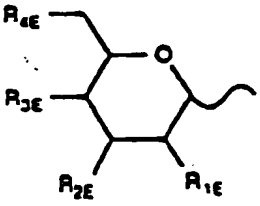
If

wherein

Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} independently are O, S, CH_2, or NR_{25}, where R_{25} is hydrogen, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl optionally substituted with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

Y is  ; A is  ;

B is  ; C is  ;

D is  ; E is  ;

wherein

the wavy line in Y, A, B, C, D and E signifies a bond which is either in the α- or in the β-configuration;

R_1, R_2, and R_3 each independently are H, halogen, azido, guanidinyl, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl or aryl-C_{1-4}-alkyl optionally substituted in the aryl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4}-alkyl)silylethyl; oxo; a group $=CR_4R_5$ wherein R_4 and R_5 independently are H, or C_{1-4}-alkyl; or a group XR_{10} wherein X is O, S, NR_{20}, or =N-, and R_{10} is H, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl, aryl-C_{1-4}-alkyl, or heterocyclyl-C_{1-4}-alkyl optionally substituted in the aryl or heterocyclyl moiety with hydroxy, amino,

C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4} alkyl)silylethyl; tri(C_{1-4}-alkyl)silyl; tri(C_{1-4}-alkyl)silylethoxymethyl; the acyl residue of a naturally occurring amino acid; C_{1-24}-alkylcarbonyl; C_{2-24}-alkenylcarbonyl; C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl; arylcarbonyl; or terpenyl; and

R_{20} is H, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl or phthaloyl optionally substituted in the benzene ring with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} each independently is as defined for R_1, R_2, and R_3 above, or is a group of the formula VII

$$YZ_1 \qquad \text{VII}$$

wherein Y and Z_1 are as defined above;
with the provisos
that one of R_{1B}, R_{2B}, R_{3B}, or R_{4B} is Z_3, Z_5, Z_8 or Z_{12}, that one of R_{1C}, R_{2C}, R_{3C}, or R_{4C} is Z_6, Z_9 or Z_{13}, that one of R_{1D}, R_{2D}, R_{3D}, or R_{4D} is Z_{10}, or Z_{14}, that one of R_{1E}, R_{2E}, R_{3E}, or R_{4E} is Z_{15}, that at least one and at the most five of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} is a group of the formula VII, and
that the configurations of the substituents R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A, the configurations of the substituents R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B, the configurations of the substituents R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C, the configurations of the substituents R_{1D}, R_{2D}, R_{3D}, and $R_{4D}CH_2$ in D, and the configurations of the substituents R_{1E}, R_{2E}, R_{3E}, and $R_{4E}CH_2$ in E independently are D-gluco, L-gluc , D-galacto,

L-galact , D-mann , L-mann , D-talo, L-talo, D-all , L-allo, D-altro, L-altro, D-gulo, L-gulo, D-ido, or L-ido;

R is a branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, C_{1-12}-alkoxy-C_{1-12}-alkyl, C_{1-24}-alkylcarbonyl, C_{2-24}-alkenylcarbonyl, or C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; an aryl, aryl-C_{1-4}-alkyl, arylcarbonyl or aryl-C_{1-4}-alkylcarbonyl group optionally substituted in the aryl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; terpenyl; tri(C_{1-4}-alkyl)silylethyl; heterocyclyl; heterocyclyl-C_{1-4}-alkyl; or heterocyclyl-C_{1-4}-alkylcarbonyl;

a group of the formula II or IIa

$$R_{30}-(CH_2)_q-S(O)_m-CH_2CH_2- \qquad II$$
$$[R_{30}-(CH_2)_q-S(O)_m-CH_2]_2CH-CH_2- \qquad IIa$$

wherein R_{30} is H, carboxy, C_{1-4}-alkoxycarbonyl, hydroxy, amino, or a matrix MA, q is an integer from 1 to 24, and m is 0 or 2; or

a group of the formula III or IIIa

$$Phe-S(O)_m-CH_2CH_2- \qquad III$$
$$[Phe-S(O)_m-CH_2]_2CH-CH_2- \qquad IIIa$$

wherein m is as defined above, and each Phe is phenyl optionally substituted with hydroxy, amin , C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy r mono- or di-halogen C_{1-4}-alkyl; or phenyl-C_{1-4}-alkyl optionally m nosubstitut d in the phenyl moiety

with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, ph n xy, or m no- or di-halogen-C_{1-4}-alkyl;

a group of the formula IV

$$R_{40}CH_2CH(CH_2R_{50})CH_2- \qquad IV$$

wherein R_{40} and R_{50} independently are halogen; or

a group Q-(Spacer)$_r$-, where r is an integer 0 or 1, and Q is a matrix MA or a group -COO-MA;

in therapy, especially for the treatment or prophylaxis in humans of conditions involving infection by *Helicobacter pylori* of human gastric mucosa. Another aspect of the invention relates to the use of said compounds for the preparation of pharmaceutical compositions for use against the above mentioned conditions.

DETAILED DESCRIPTION OF THE INVENTION

In the present context, the terms "C_{1-4}-alkyl", "C_{1-8}-alkyl" and "C_{1-24}-alkyl" as a separate group or as part of a group designates alkyl groups with 1-4, 1-8 or 1-24 carbon atoms which may be straight or branched such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert.butyl, dimethylbutyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, hexadecyl, octadecyl, etc.
In the carbon chain the definition "C_{1-24}-alkyl" is used herein, but also shorter number of carbon atoms in the carbon chain is possible as "C_{1-8}-alkyl" or "C_{1-4}-alkyl".
The term "C_{1-4}-alkyl" is used herein when substituents are defined.
The term "C_{3-8}-cycloalkyl" as a group or as part of a group designates a cyclic alkyl group with 3-8 carbon atoms such as

cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl.

The term "C_{2-24}-alkenyl" designates unsaturated alkyl groups with 2-24 carbon atoms which may be straight or branched, preferably straight, in which the double bond may be present anywhere in the chain, for example vinyl, 1-propenyl, 2-propenyl, hexenyl, decenyl, hexadecenyl, octadecenyl. The term "C_{2-24}-alkynyl" designates an alkyl group with 2-24 carbon atoms and incorporating a triple bond, e.g. ethynyl, 1-propynyl, 2-propynyl, 2-butynyl etc. The term "halogen" designates Cl, Br, I and F, preferably F and Cl.

The terms "C_{1-4}-alkoxy" and "C_{1-24}-alkoxy" designate groups comprising an oxa function substituted with an alkyl group as defined above.

The terms "aryl" and "aryloxy", either as a separate group or as part of a group, designates phenyl or naphthyl, preferably phenyl.

The term "aryl-amide" defines either aryl-NH-C(O)- e.g. anilids, or aryl-C(O)-NH- e.g.benzamide.

The term "terpenyl moiety" designates groups derived from some of the various unsaturated hydrocarbon compounds generically known as the terpenes, namely the monoterpenes and the sesquiterpenes, as well as hydroxy or oxo derivatives thereof. Examples of such groups are myrcenyl, (-)-limonenyl, terpineloyl, (+)-α-pinenyl, geraniolyl, (-)-mentholyl, (-)-camphoryl, farnesolyl, β-eudesmolyl, and manoolyl.

In the present context, the term "oligosaccharide" designates an oligosaccharide containing 4-10 monosaccharide units, preferably 4-7 monosaccharide units, the monosaccharide units being selected from aldohexoses (i.e. D-glucose, L-glucose, D-galactose, L-galactose, D-mannose, L-mannose, D-talose, L-talose, D-allos , L-allose, D-altrose, L-altros , D-gul se, L-gulose, D-id se, r L-idose) or their derivatives, where the oligosaccharide may be linear or branch d with the proviso that

there are no more than seven monosaccharide units in the longest chain in the oligosaccharide.

As indicated above, the wavy lines on the carbon atoms neighbouring the ring oxygen atoms in groups Y, A, B, C, D, and E signify that the bonds in question which are glycosidic bonds have either the α- or the β-configuration. It is clear that each of the bonds in question on a particular group Y, A, B, C, D, and E may assume the α- or the β-configuration independent of the corresponding bonds on the other groups.

A mono- or di-halogen-C_{1-4}-alkyl group may be substituted in any position and if substituted with 2 halogen atoms, the halogen atoms may be the same or different.

The term "heterocyclyl" designates a monocyclic 5- or 6-membered, or a fused bicyclic (each ring being 5- or 6-membered), aromatic or partly or fully saturated heterocyclic group containing from one to four hetero atoms per ring, the heteroatoms being selected independently from O, S and N and bound either *via* a carbon atom or *via* a nitrogen atom. Typical but non-limiting examples of such groups may comprise pyrrolyl, pyrazolyl, pyridinyl, thienyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, isothiazolyl, furyl, pyrazinyl, pyrimidinyl, pyridazinyl, 2H-1,3-oxazinyl, 4H-1,3-oxazinyl, 6H-1,3-oxazinyl, 2H-1,3-thiazinyl, 4H-1,3-thiazinyl, 6H-1,3-thiazinyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, 1H-1,2,4-triazolyl, 4H-1,2,4-triazolyl, indolyl, purinyl, piperidyl or piperidino, morpholinyl or morpholino, piperazinyl, tetrahydrofuryl, thiazolidinyl, oxazolidinyl, imidazolidinyl, isoxazolidinyl, isothiazolidinyl, pyrrolidinyl, 1H-tetrazolyl, or 2H-tetrazolyl.

The term "acyl residue of a naturally occurring amino acid" designates the acyl residue of the L-amino acids occurring in proteins in nature, e.g. alanyl, valyl, leucyl, isoleucyl, prolinyl, phenylalanyl, tryptophanyl, methionyl, glycyl, seryl, threonyl, cysteinyl, tyrosyl, asparagyl, glutamyl, lysyl,

arginyl, histidyl and the acyl residues of aspartic acid and glutamic acid, the acyl residue referring both t th carboxy group next to the amino function as well as the carboxy group at the end of the respective side chains, preferably, however, the carboxy groups next to the amino functions.

The term "sphingoid" refers to D-erythro-2-amino-1,3-octadecanediol, its homologs and stereoisomers and to hydroxy and unsaturated derivatives thereof, including ceramide (see further definitions in Journ. of Lipid Research, vol. 19, (1978), 617-631).

The term "steroid" refers to well-known steroids as cholesterol, cortisone, hydrocortisone, corticosterone, betamethasone, prednosolone, prednisone etc.

The term "matrix" as used herein and designated as "MA" signifies any organic or inorganic, polymeric or macromolecular structure to which the aglycon part of the O-, S-, C-, or N-glycosidic compound of the formula Ia, Ib, Ic, Id, Ie or If is attached either covalently or by e.g. hydrophobic interaction. Examples of such matrices are residues of proteins, glycoproteins, polypeptides, polysaccharides, liposomes, emulsions, plastic polymers and inorganic materials. Residues of proteins are preferably bonded through nucleophilic groups in the proteins, e.g. groups such as amino, hydroxyl and mercapto groups. Proteins or polypeptides themselves may be any of a wide variety of substances, in particular biologically compatible proteins such as globulins, albumins such as human serum albumin (HSA), bovine serum albumin (BSA) or sheep serum albumin (SSA), ovalbumin, fibrins, or "key-hole" limpet haemocyanin (KLH), glycoproteins such as bovine or human whole casein or lectins, and the like. Other examples of such matrices are synthetic polymers where one or several amino acids are coupled to a polymer of defined size(s), e.g. polylysine or olig lysine. In the vari us pr teins or polypeptides, the linkag to the remainder f the group R may be through amino groups or through carboxyl gr ups.

The polysaccharides, to which the O-, S-, C-, or N-glycosidic compounds are attached, may be any of a wide variety of polysaccharides. The aglycon part of the compound of formula Ia, Ib, Ic, Id, Ie or If may be bonded through hydroxyl groups on ordinary polysaccharides such as cellulose, sepharose, starch or glycogen, through amino groups on amino saccharides such as chitosane or aminated sepharose, and through mercapto groups of thio-modified polysaccharides.

Liposomes may be any biocompatible, biodegradable microesicular system compose of one or several bilayers surrounding aqueous compartments, within which a variety of agents can be encapsulated: hydrophobic agents in the lipid bilayers and hydrophilic agents in the inner aqueous space. The physicochemical properties of the liposomes are mainly dependent on the lipid composition.

Liposomes are composed of phospholipids, such as egg yolk phospholipids, soya phospholipids, synthetic phosphatidylcholine e.g dimyritoylphosphatidylcholine (DMPC) and/or dipalmtoylphosphartidylchlorine (DPPC) or purified phosphatidylcholines of vegetable origin or other lipids, such as galactolipids, sphingolipids or glycosphingolipids.

Emulsions are heterogenous mixtures of two or more imiscible liquids. To stabilize these systems an emulsifier is added. The emulsifier is oriented at the interface of the imisible liquids and usually only one phase persist in dropted form.

Emulsions fall into two general categories. The heterogenous system described by droplets of an organic liquid dispersed in a continuous water phase is called oil-in-water emulsion (o/w). Alternatively, the heterogenous system described by droplets of water dispersed in a continuous oil phase is called water-in-oil emulsion (w/o).

Any vegetable oil such as soybean oil, safflower oil, sesame oil, peanut oil, cottonseed oil, borago oil, sunflower oil,

corn oil, olive oil, medium chain triglycerides (such as Miglyol ®), or acetylated monoglycerides may be used as internal or continuous phase.

Examples of plastics to which the aglycon part of the compounds of the formula Ia, Ib, Ic, Id, Ie or If may be attached are aminated latex, thiolated, aminated, or hydroxylated polystyrene, polyacrylamide and polyvinyl alcohol. Other possible carriers are beads and gels of carbohydrate origin or polymers where carbohydrates are used in combination with other polymeric materials such as sephacryl. These gels are further substituted with groups such as amino, thiols, cyano, active esters and disulfides. The plastics in question may be in the form of e.g. beads or film.

Examples of inorganic material, to which the aglycon part of the compounds of the formula Ia, Ib, Ic, Id, Ie or If may be attached are silicon oxide materials such as silica gel, zeolite, diatomaceous earth, or the surface of various glass or silica gel types such as thiolated or aminated glass, where the silica gel or the glass may be in the form of e.g. beads. Another example of an inorganic material is aluminium oxide.

Particularly preferred matrix MA is human serum albumin (HSA), bovine serum albumin (BSA) and polyacrylamide (PAA).

An interesting embodiment of the invention is when the compound of formula Ia, Ib, Ic, Id, Ie or If comprises a matrix MA, said matrix incorporating a multiplicity (i.e. 2 or more, such as 2-100 when the matrix is a protein such as BSA or HSA, or 10-10,000 when the matrix is a polymer such as polyacrylamide) f moieties of the formula Ia, Ib, Ic, Id, Ie and If. It is contemplated that the presence of several such moieties will substantially enhance the inhibiting effect of the entire compound due to a multivalency-effect thereof on the bacteria. It is also possible that the presence of several moieties of the formula Ia, Ib, Ic, Id, Ie and If may even lead to agglutinati n of the bacteria.

When, in connection with the definiti n of formulas Ia, Ib, Ic, Id, Ie and If, it is stated that the c nfigurations of the substituents R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A, the configurations of the substituents R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B, the configurations of the substituents R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C, the configurations of the substituents R_{1D}, R_{2D}, R_{3D}, and $R_{4D}CH_2$ in D, and the configurations of the substituents R_{1E}, R_{2E}, R_{3E}, and $R_{4E}CH_2$ in E independently are D-gluco, L-gluco, D-galacto, L-galacto, D-manno, L-manno, D-talo, L-talo, D-allo, L-allo, D-altro, L-altro, D-gulo, L-gulo, D-ido, or L-ido, this is intended to mean that the stereochemical substitution patterns that can be assumed by the various R-groups or R-group-containing groups on the cyclic groups A, B, C, D and E correspond to the stereochemical patterns formed by the 2-, 3-, and 4-hydroxy groups and the 5-hydroxymethyl group in D-glucose, L-glucose, D-galactose, L-galactose, D-mannose, L-mannose, D-talose, L-talose, D-allose, L-allose, D-altrose, L-altrose, D-gulose, L-gulose, D-idose, or L-idose, respectively.

It will be clear that the groups R_1, R_2, R_3 and CH_3 in the group Y are arranged in such a configuration to give a L-galacto-pyranosyl unit and that the group Y therefore is a L-fucose unit or a derivative thereof.

In the compounds of the formula Ia, Ib, Ic, Id, Ie or If, it is preferred that Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} are O.

It is also preferred that at the most four, more preferably at the most three, in particular one or two of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, or R_{4E} is a group of formula VII.

It is also preferred that R_{1A} is a group VII in the α-configuration.

It is als preferred that the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration.

Particularly preferred compounds are those wherein R_{1A} is a group VII in the α-configuration and the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration, especially A is Fucα1-2Galβ.

It is also preferred that R_{2B} is Z_3, Z_5, Z_8, or Z_{12}, and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration.

It is also preferred that R_{1B} is an acetamido group.

Particularly preferred compounds are those wherein R_{1A} is a group VII in the α-configuration; the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration; R_{2B} is Z_3, Z_5, Z_8, or Z_{12}; and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration and R_{1B} is an acetamido group.

Especially interesting are those compounds in which the A-Z_3-B is Fucα1-2Galβ1-3GlcNAcβ or Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ, those compounds in which A-Z_5-B-Z_6-C is Fucα1-2Galβ1-3GlcNAcβ1-3Galβ or Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ, those compounds in which A-Z_8-B-Z_9-C-Z_{10}-D is GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ or Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glc$\beta$and those compounds in which A-Z_{12}-B-Z_{13}-C-Z_{14}-D-Z_{15}-E is GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ.

It is also preferred that R_{3B} is a group of the formula VII in the α-configuration.

Particularly preferred compounds are those wherein the configurations of R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A and of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-galact , and the configurations of

R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C are D-gluco, A b ing in the α-configuration, and B and C being in the β-configuration, and in which R_{1B} and R_{3C} are groups of the formula VII in the α-configuration, and in which R_{1A} and R_{1C} are acetamido groups, and R_{2B} is Z_5, Z_8 or Z_{12}, and R_{2C} is Z_6, Z_9 or Z_{13}.

An interesting class of compounds is that in which the carbohydrate moiety contains the structure Y-Z_1-A- where Z_1 is O and the L-fucose unit Y is linked to the 2-position of A. Examples of interesting basic carbohydrate structures in this class are those having the following formulae where the substituents R_1, R_2, R_3, R_{1A}, R_{2A}, R_{3A}, and R_{4A} each are indicated as OH, although this is not to be construed as limiting the definitions of the R-substituents in this manner; rather, R_1, R_2, R_3, R_{1A}, R_{2A}, R_{3A}, and R_{4A} should be considered as being able to assume all the meanings defined above in connection with the formulae Ia, Ib, Ic, Id, Ie and If. Thus, the structure Y-Z_1-A- may be

Fucα1-2Allβ1→
Fucα1-2Altβ1→
Fucα1-2Glcβ1→
Fucα1-2Manβ1→
Fucα1-2Gulβ1→
Fucα1-2Idoβ1→
Fucα1-2Galβ1→
Fucα1-2Talβ1→

When the groups R_1, R_2, R_3, R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, or R_{4E} in Y, A, B, C, D, and E are not hydroxyl, they may preferably be selected among the following:

H, Cl, F, azido, guanidyl, methyl, ethyl, propyl, vinyl, allyl, prop-1-enyl, ethynyl, prop-2-ynyl, prop-1-ynyl, acetyl, cyclopropyl, cyclopropylmethyl, methoxymethyl, hydroxymethyl, phenyl, oxo, methylene, thiol, amin , methoxy, ethoxy, propoxy, butoxy, hexyloxy, decyloxy, tetradecyloxy, octadecyloxy, vinyloxy, allyloxy, 1-propen-1-yloxy, crotyl xy,

3-buten-1-yloxy, 2-hexen-1-yloxy, 5-hexen-1-yl xy, 5-decen-1-yloxy, 9-decen-1-yloxy, 11-tetrad cen-1-yloxy, oleoyl, ethynyloxy, 2-propyn-1-yloxy, 1-propyn-1-yloxy, methylthio, methylamino, dimethylamino, cyclopropoxy, cyclopropylmethoxy, methoxymethoxy, phenoxy, benzyloxy, 2-furylmethoxy, 2-thienylmethoxy, 2-pyridylmethoxy, trimethylsilyloxy, trimethylsilylethoxy, acetoxy, propionyloxy, butyryloxy, hexanoyloxy, decanoyloxy, tetradecanoyloxy, octadecanoyloxy, acetamido, N-methylacetamido, acetylthio, glycyloxy, or alanyloxy.

Interesting examples of aglycon groups R are the following: Methyl, ethyl, propyl, isopropyl, butyl, sec.butyl, isobutyl, tert.butyl, pentyl, isopentyl, 2-methylbutyl, 1-methylbutyl, 1-ethylpropyl, hexyl, isohexyl, 3-methylpentyl, 2-methylpentyl, 1-methylpentyl, 2-ethylbutyl, 1-ethylbutyl, heptyl, isoheptyl, 4-methylhexyl, 3-methylhexyl, 2-methylhexyl, 1-methylhexyl, 3-ethylpentyl, 2-ethylpentyl, 1-ethylpentyl, 1-propylbutyl, octyl, decyl, dodecyl, tetradecyl, hexadecyl, octadecyl, tetracosyl, cyclopropyl, cyclopropylethyl, cyclobutyl, cyclobutylmethyl, cyclopentylmethyl, cyclopentylprop-3-yl, cyclohexyl, cyclohexylmethyl, cyclohexylprop-3-yl, cycloheptyl, phenyl, 4-nitrophenyl, benzyl, 4-phenylprop-1-yl, 3-hexylthio-2-(hexylthio)methylprop-1-yl, 3-hexylsulfonyl-2-(hexylsulfonyl)methylprop-1-yl, 3-decylthio-2-(decylthio)methylprop-1-yl, 3-decylsulfonyl-2-(decylsulfonyl)methylprop-1-yl, 8-amino-3,6-dioxaoct-1-yl, 1,3-dihydroxyprop-2-yl, 1,3-diaminoprop-2-yl, 3-hydroxy-2-(hydroxymethyl)prop-1-yl, 2-phenylthioethyl or trimethylsilylethyl.

In a group R comprising a matrix MA, the linkage between the matrix MA and the remainder of R may typically be through any of the spacers well known in the field of protein conjugates, cf. for example J.H. Pazur, *Adv. Carbohydr. Chem. Biochem.*, Vol 39, (1980), 405-447; Y.C. Le & R.T. Lee, "Glycoconjugates", V 1. 4 Part B, 57-83, Ed. Horowitz, Academic Press, N.Y. (1982); and G. Magnusson, FEMS Symposium, 215-228 (1986). In

the present context, th term "Spacer" is intended to mean a molecule moiety which links the active substance to a carrier. A spacer molecule is designed t have two different functionalities, each reacting specifically with another functionality, a linear moiety being placed between these two functionalities. By linking the active substance to a carrier *via* a Spacer, one makes the active substance more accessible, e.g. to *H. pylori* adhesins or colonization factor antigens.

The Spacer can be defined as $(W)_v$-S'-P', wherein S' is an C_{1-24} alkyl, an C_{2-24} alkenyl, an C_{1-24}alkylaryl, an arylC_{1-24}alkyl an arylC_{1-24}alkylaryl, an C_{1-24}alkylarylC_{1-24}alkyl group which groups may be interrupted by carbonyl, thiocarbonyl, oxycarbonyl, carbonyloxy, carbonylamino, aminocarbonyl, aza, oxa or thia groups; an aryl group, an aryloxy, an C_{1-24}alkoxy, a polyethyleneglycol group, a steroid group, a sphingoid group; all groups may be substituted with carboxyl, C_{1-4}alkylcarbonyl, amide, hydroxy, alkoxy, aryloxy, phenoxy;

P' is NH-C(S), NH-C(O), C(O), NH, C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_3, PO_4;
W is NH-C(S), NH-C(O), C(O), C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_2, PO_3, PO_4,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are CH_2 then W cannot be PO_2,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are O or S then W cannot be (O)CO, SO_4 or PO_4, and with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are NH then W cannot be NH-C(S), NH-C(O), (O)CO, SO_4, PO_4; and v is an integer 0 or 1.

The atom of the sugar moiety which linkages to the spacer is selected among from the following: -O-, -S-, -NH-, $-CH_2-$ preferably -O-.

In the compounds of the formulas Ia, Ib, Ic, Id, Ie and If, the various groups R carrying the matrix MA may th mselves comprise the spacer and the linkage. Specific and typical exampl s of linkag s ar those formed through amino group- or keto group-

containing matrices. Such linkages between th spacer and the matrix may hav the following general structur s:

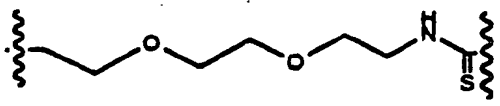
-NH-C(S)-***NH***- or -C(O)-***NH***-, or -NH-***C(O)***-

wherein the atoms marked ***bold and italic*** orginate from the given matrix.

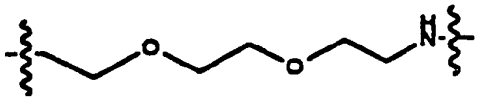
The number of structures of the formulas Ia, Ib, Ic, Id, Ie or If on each matrix unit may be mono- or multivalent and may vary between 1 to 10,000, depending on the nature of the matrix.

Below follow a non-limiting list of examples of spacers suitable between Q and the remainder of R

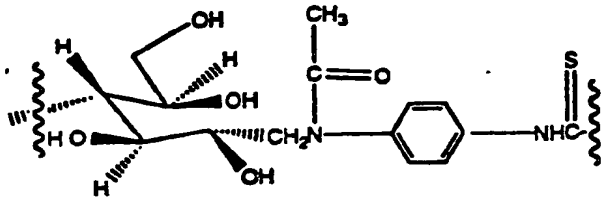
spacer 1



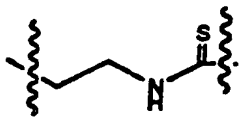
spacer 2



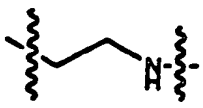
spacer 3



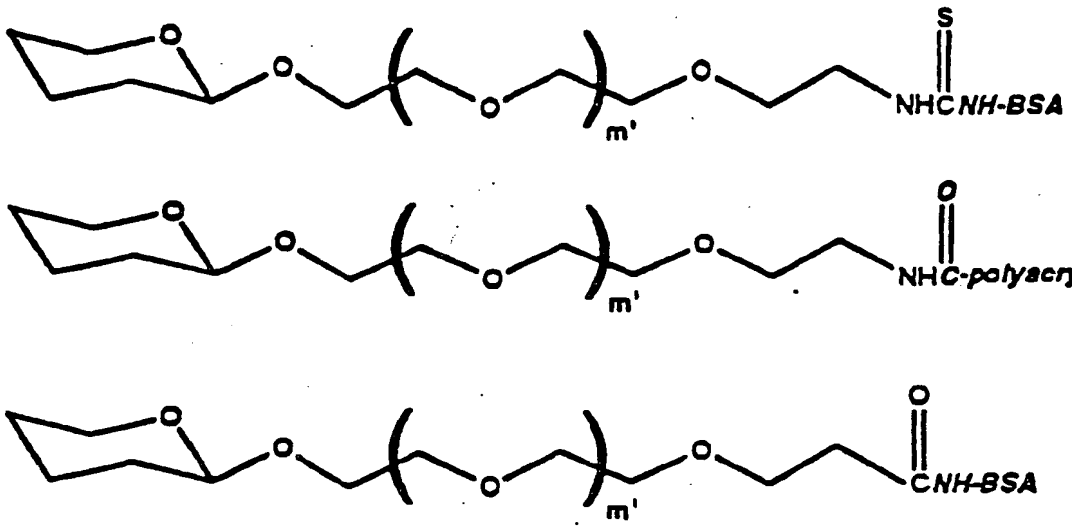
spacer 4

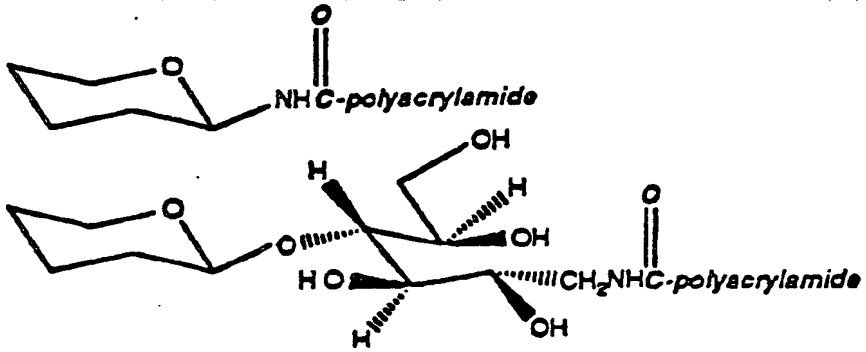


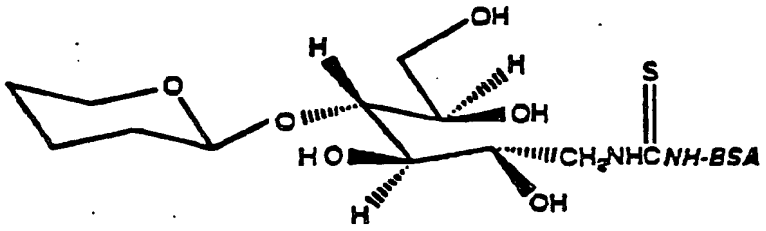
spacer 5

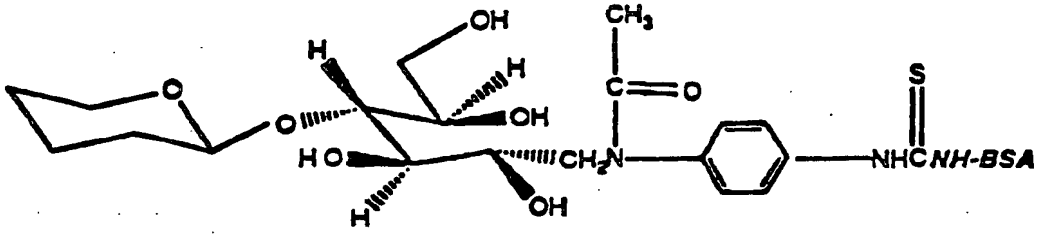


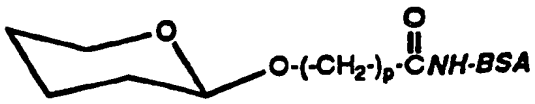
In the list of spacers given above and below, the atoms marked in bold italics originate from the matrix in question. The vertical wavy lines on the left and right ends in the spacer above signify that there are bonds at the ends. As examples of compounds f th general formulas Ia, Ib, Ic, Id, Ie r If comprising matrix moi ties, the f llowing may be mentioned:

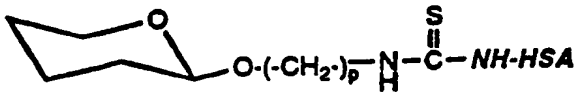

S
NHC NH-BSA
m'
O
NHC-polyacrylamide
m'
O
CNH-BSA
m'

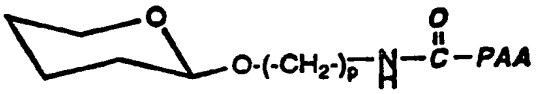

O
NHC-polyacrylamide
OH
H
H
OH
O
HO
CH2NHC-polyacrylamide
O
H
OH

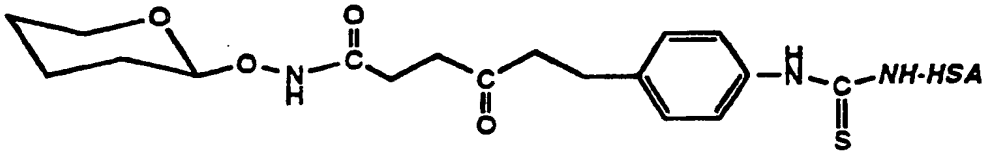

OH
H
H
OH
O
HO
S
CH2NHC NH-BSA
H
OH

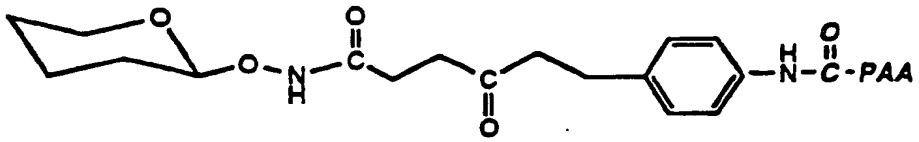

OH
CH3
H
H
C
O
OH
O
HO
S
CH2N
NHC NH-BSA
H
OH

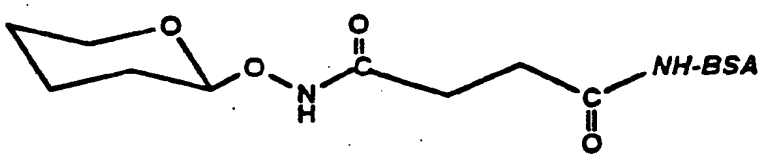

O-(-CH2-)p-CNH-BSA


O-(-CH2-)p-NH-C-NH-HSA


O-(-CH2-)p-NH-C-PAA


NH-HSA


PAA


NH-BSA

When  is used in the examples above, this has the meaning of mono-, di-, tri- or oligosaccharide as specified in the text, and m' is an integer 0-5 and p is an integer 0-13.

When the matrix above is exemplified by BSA, HSA and polyacrylamide(PAA) this can be any other protein or peptide or other matrix specified in the text.

Specific examples of interesting compounds of the formula Ia, Ib, Ic, Id, Ie or If are the following:

Fucα1-2Galβ1-O-propyl
Fucα1-2Galβ1-O-isopropyl
Fucα1-2Galβ1-O-butyl
Fucα1-2Galβ1-O-tert-butyl
Fucα1-2Galβ1-O-hexyl
Fucα1-2Galβ1-O-octyl
Fucα1-2Galβ1-O-decyl
Fucα1-2Galβ1-O-tetradecyl
Fucα1-2Galβ1-O-octadecyl

Fucα1-2Galβ1-O-(C_6bissulfide)
Fucα1-2Galβ1-O-(C_{10}bissulfide)
Fucα1-2Galβ1-O-(C_6bissulfone)
Fucα1-2Galβ1-O-(C_{10}bissulfone)
Fucα1-2Galβ1-O-(8-amino-3,6-dioxaoct-1-yl)

Fucα1-2Galβ1-3GlcNAcβ1-O-propyl
Fucα1-2Galβ1-3GlcNAcβ1-O-isopropyl
Fucα1-2Galβ1-3GlcNAcβ1-O-butyl
Fucα1-2Galβ1-3GlcNAcβ1-O-tert.butyl
Fucα1-2Galβ1-3GlcNAcβ1-O-hexyl
Fucα1-2Galβ1-3GlcNAcβ1-O-octyl
Fucα1-2Galβ1-3GlcNAcβ1-O-decyl
Fucα1-2Galβ1-3GlcNAcβ1-O-tetradecyl
Fucα1-2Galβ1-3GlcNAcβ1-O-octadecyl

Fucα1-2Galβ1-3GlcNAcβ-1-O-(C_6bissulfide)

Fucα1-2Galβ1-3GlcNAcβ-1-O-(C_6bissulfone)
Fucα1-2Galβ1-3GlcNAcβ-1-O-(8-amino-3,6-dioxaoct-1-yl)

Fucα1-2Galβ1-3Glcβ1-O-propyl
Fucα1-2Galβ1-3Glcβ1-O-isopropyl
Fucα1-2Galβ1-3Glcβ1-O-butyl
Fucα1-2Galβ1-3Glcβ1-O-tert.butyl
Fucα1-2Galβ1-3Glcβ1-O-hexyl
Fucα1-2Galβ1-3Glcβ1-O-octyl
Fucα1-2Galβ1-3Glcβ1-O-tetradecyl
Fucα1-2Galβ1-3Glcβ1-O-octadecyl

Fucα1-2Galβ1-3Glcβ1-O-(C_6bissulfide)
Fucα1-2Galβ1-3Glcβ1-O-(C_6bissulfone)
Fucα1-2Galβ1-3Glcβ1-O-(8-amino-3,6-dioxaoctyl)

wherein

C_6bissulfide = 3-hexylthio-2-(hexylthio)methylprop-1-yl-
C_{10}bissulfide = 3-decylthio-2-(decylthio)methylprop-1-yl-
C_6bissulfone = 3-hexylsulfonyl-2-(hexylsulfonyl)methylprop-1-yl-
C_{10}bissulfone = 3-decylthio-2-(decylthio)methylprop-1-yl-

Further interesting compounds are:

Fucα1-2Galβ1-O-Me
Fucα1-3Glcβ1-O-Me
Fucα1-3GlcNAcβ1-O-Me
Fucα1-3GlcNAcβ1-Spacer 1-BSA
Fucα1-3GlcNAcβ1-O tetradecyl
Fucα1-4GlcNAcβ1-O-Me
Fucα1-4GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-4GlcNAcβ1-O-tetradecyl
Fucα1-4Galβ1-O-Me
Fucα1-6Galβ1-O-Me
Fucα1-6Galβ1-Spacer 2-p lyacrylamide
Fucα1-2Galβ1-Spac r 2-polyacrylamide

Fucα1-2Galβ1-Spacer 1-BSA
Fucα1-2Galβ1-Spacer 1-HSA
Fucα1-2Galβ1-Spacer 4-BSA
Fucα1-2Galβ1-Spacer 4-HSA
Fucα1-2Galβ1-Spacer 5-polyacrylamide .
Fucα1-2Galβ1-O-tetradecyl
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 5-polyacrylamide
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 4-BSA
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 4-HSA
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 1-HSA
Fucα1-2Galβ1-3GlcNAcβ1-Spacer 1-BSA
Fucα1-2Galβ1-3GlcNAcβ1-O-tetradecyl
Fucα1-2Galβ1-3Glcβ1-Spacer 1-HSA
Fucα1-2Galβ1-3Glcβ1-Spacer 1-BSA
Fucα1-2Galβ1-3Glcβ1-Spacer 4-HSA
Fucα1-2Galβ1-3Glcβ1-Spacer 4-BSA
Fucα1-2Galβ1-3Glcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-3Glcβ1-Spacer 5-polyacrylamide
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 1-HSA
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 1-BSA
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 4-HSA
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 4-BSA
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-3(Fucα1-4)Glcβ1-Spacer 5-polyacrylamide
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer 3-BSA
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer 5-polyacrylamide
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-O-tetradecyl
Fucα1-2Galβ1-4Glcβ1-Spacer 1-BSA
Fucα1-2Galβ1-4Glcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-4Glcβ1-O-tetradecyl
Galβ1-4(Fucα1-3)GlcNAcβ1-Spacer 1-BSA
Galβ1-4(Fucα1-3)GlcNAcβ1-Spacer 2-polyacrylamide
Galβ1-4(Fucα1-3)GlcNAcβ1-O-tetradecyl
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 3-BSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 3-HSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 5-polyacrylamide

Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 1-HSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 5-BSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 4-HSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 4-BSA
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-O-tetradecyl
GalNAcα1-3(Fucα1-2)3Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer-3-BSA
GalNAcα1-3(Fucα1-2)3Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer-2-polyacrylamide
GalNAcα1-3(Fucα1-2)3Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-O-tetradecyl
Fucα1-2Galβ1-4(Fucα1-3)Glcβ1-Spacer 1-BSA
Fucα1-2Galβ1-4(Fucα1-3)Glcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-4(Fucα1-3)Glcβ1-O-tetradecyl
Fucα1-2(3-O-methyl)Galβ1-O-tetradecyl
Fucα1-2(3-O-methyl)Galβ1-Spacer 1-BSA
Fucα1-2(3-O-methyl)Galβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-allyl)Galβ1-Spacer 1-BSA
Fucα1-2(3-O-allyl)Galβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-allyl)Galβ1-O-tetradecyl
Fucα1-2(3-O-propyl)Galβ1-Spacer 1-HSA
Fucα1-2(3-O-propyl)Galβ1-Spacer 1-BSA
Fucα1-2(3-O-propyl)Galβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-propyl)Galβ1-Spacer 4-HSA
Fucα1-2(3-O-propyl)Galβ1-Spacer 4-BSA
Fucα1-2(3-O-propyl)Galβ1-Spacer 5-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-Spacer 1-BSA
Fucα1-2(3-O-butyl)Galβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-O-tetradecyl
Fucα1-2(3-O-methyl)Galβ1-3GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-methyl)Galβ1-3GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-methyl)Galβ1-3GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-allyl)Galβ1-3GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-allyl)Galβ1-3GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-allyl)Galβ1-3GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-propyl)Galβ1-3GlcNacβ1-Spacer 1-HSA
Fucα1-2(3-O-propyl)Galβ1-3GlcNacβ1-Spacer 1-BSA

Fucα1-2(3-O-pr pyl)Galβ1-3GlcNacβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-propyl)Galβ1-3GlcNacβ1-Spacer 4-HSA
Fucα1-2(3-O-propyl)Galβ1-3GlcNacβ1-Spacer 4-BSA
Fucα1-2(3-O-propyl)Galβ1-3GlcNacβ1-Spacer 5-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-3GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-butyl)Galβ1-3GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-3GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 1-HSA
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 1-BSA
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 4-HSA
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 4-BSA
Fucα1-2(3-O-propyl)Galβ1-3(Fucα1-4)GlcNacβ1-Spacer 5-polyacrylamide
Fucα1-2(3-O-methyl)Galβ1-4GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-methyl)Galβ1-4GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-methyl)Galβ1-4GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-allyl)Galβ1-4GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-allyl)Galβ1-4GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-allyl)Galβ1-4GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-butyl)Galβ1-4GlcNAcβ1-Spacer 1-BSA
Fucα1-2(3-O-butyl)Galβ1-4GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-4GlcNAcβ1-O-tetradecyl
Fucα1-2(3-O-methyl)Galβ1-3Glcβ1-Spacer 1-BSA
Fucα1-2(3-O-methyl)Galβ1-3Glcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-methyl)Galβ1-3Glcβ1-O-tetradecyl
Fucα1-2(3-O-allyl)Galβ1-3Glcβ1-Spacer 1-BSA
Fucα1-2(3-O-allyl)Galβ1-3Glcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-allyl)Galβ1-3Glcβ1-O-tetradecyl
Fucα1-2(3-O-butyl)Galβ1-3Glcβ1-Spacer 1-BSA
Fucα1-2(3-O-butyl)Galβ1-3Glcβ1-Spacer 2-polyacrylamide
Fucα1-2(3-O-butyl)Galβ1-3Glcβ1-O-tetradecyl
Fucα1-2Galβ1-4GlcNAcβ1-Spacer 1-BSA
Fucα1-2Galβ1-4GlcNAcβ1-Spacer 2-polyacrylamide
Fucα1-2Galβ1-4GlcNAcβ1-O-tetradecyl
Galα1-3(Fucα1-2)Galβ1-Spacer 1-BSA
Galα1-3(Fucα1-2)Galβ1-Spacer 2-polyacrylamide

Galα1-3(Fucα1-2)Galβ1-O-tetradecyl
GalNAcα1-3(Fucα1-2)Galβ1-4Glcβ1-Spacer 1-BSA
GalNAcα1-3(Fucα1-2)Galβ1-4Glcβ1-Spacer 2-polyacrylamide
GalNAcα1-3(Fucα1-2)Galβ1-4Glcβ1-O-tetradecyl
Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-Spacer 1-BSA
Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-Spacer 2-polyacrylamide
Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-O-tetradecyl
Galβ1-3(Fucα1-4)GlcNAcβ1-Spacer 1-BSA
Galβ1-3(Fucα1-4)GlcNAcβ1-Spacer 2-polyacrylamide
Galβ1-3(Fucα1-4)GlcNAcβ1-O-tetradecyl

In the present application, such as the list above, specific compounds or parts of compounds may be named or represented in a condensed form corresponding to the recommendations concerning nomenclature of glycoproteins, glycopeptides, and peptidoglycans made by the Joint Commission on Biochemical Nomenclature under the International Union of Pure and Applied Chemistry and the International Union of Biochemistry (cf. *Pur & Applied Chem.*, Vol. 60, No. 9, pp 1389-1394, 1988).

In another aspect, the invention concerns a pharmaceutical composition comprising a compound of the formula Ia, Ib, Ic, Id, Ie or If as defined above or a mixture thereof in combination with at least one anti-ulcer medicament, or with at least one antibacterially active compound, or mixtures thereof, as well as a pharmaceutically acceptable carrier.

The term "anti-ulcer medicament" is intended to denote any substance or composition which is able to reduce or participate in reducing gastrointestinal ulcerations, in particular ulcerations in the stomach or duodenum. Pharmaceutical compositions according to the invention containing such substances or compositions have the potential advantage of being able to provide a dual effect by on the one hand reducing the ulceration and on the other hand simultaneously lowering the degree of infection in the stomach by *H. pylori* by preventing or inhibiting the adhesion of the bacterium ont the gastric or duodenal mucosa, th reby further promoting the

healing of an ulcer. Suitabl types of anti-ulcer medicaments are gastric secretion inhibiting compounds (primarily acid secretion inhibiting compounds) and antacids.

In a preferred aspect of the use according to the invention, the pharmaceutical composition prepared is adapted to be administered in combination with a preparation for standard therapy of gastritis or ulcus, such as preparations containing anti-ulcer or anti-gastritis medicaments, e.g. selected among gastric secretion inhibiting compounds such as omeprazole, cimetidine, ranitidine, lansoprazole, pantoprazole, sucralfate, famotidine, or nizatidine, or antacids such as magnesium hydroxide, aluminium hydroxide, calcium carbonate, sodium carbonate, sodium hydrogen carbonate, simethicone or aluminium magnesium hydroxide or a hydrate thereof (such as the monohydrate known as magaldrate).

In another preferred aspect of the use according to the invention, the pharmaceutical composition prepared is adapted to be administered in combination with a preparation for a course of therapy with an antibacterial agent, such as an antibacterial agent selected from those listed above, in particular preparations containing β-lactam antibiotics such as amoxicillin, ampicillin, cephalothin, cefaclor or cefixime; or macrolides such as erythromycin, or clarithromycin; or tetracyclines such as tetracycline or doxycycline; or aminoglycosides such as gentamycin, kanamycin or amikacin; or quinolones such as norfloxacin, ciprofloxacin or enoxacin; or others such as metronidazole, nitrofurantoin or chloramphenicol; or preparations containing bismuth salts such as bismuth subcitrate, bismuth subsalicylate, bismuth subcarbonate, bismuth subnitrate or bismuth subgallate.

In a further aspect, the invention concerns all novel compounds among those having the formula Ia, Ib, Ic, Id, Ie or If defined above.

The compounds of formula Ia, Ib, Ic, Id, Ie or If can b prepared according to several general methods using monosaccharides or oligosaccharides as starting materials. Functional group transformations can be performed before or after the formation of glycoside bonds. To ensure transformations of the functional group in a certain position, the use of reactions which are regiospecific or the protection with protective groups may optionally be necessary. The protective groups can be removed or can form part of the compound in question.

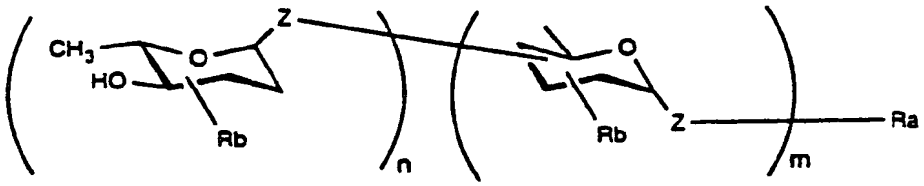
The compounds of the invention can e.g. be prepared as shown in the scheme below. In the scheme, although specific substituents or configuration may be shown, it is to be understood that to the extent that it is appropriate, the various groups shown may assume the full variability range as defined for the general formulae Ia, Ib, Ic, Id, Ie, and If.

MONOSACCHARIDES

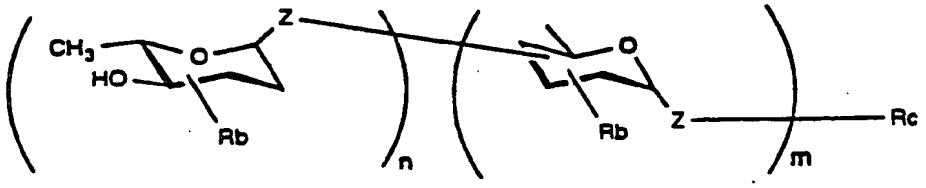
Step 1

Step 2

Step 3



Step 4



In the first step (step 1) a monosaccharide, e.g. L-fucose, D-galactose, D-glucose, 2-deoxy-2-phthalimido-D-glucos , 2-deoxy-2-phthalimido-D-galactose, D-mannose, is converted to a glycoside, with aglycons (Ra), e.g. SEt, SPh, OTMSEt, O-allyl or OBn (known aglycons in the art), to form the R_a-glycoside derivative in such a way that the R_a-glycoside is possible to transform to a glycosyl donator by activation of the anomeric centre. The Ra-glycosides can be prepared as follows: A monosaccharide as above is per-O-acylated with acetic anhydride in pyridine or with acetic anhydride-sodium acetate or with benzoyl chloride in pyridine. The monosaccharide per-O-acylate is reacted with, e.g. hydrogen bromide or hydrogen chloride in a suitable solvent such as, e.g. acetic acid or dichloromethane, to form per-O-acylated glycosyl bromide or chloride (e.g. on O-acylation and glycosyl halide synthesis, see M. L. Wolfrom and A. Thompson, *Methods in Carbohydrate Chemistry*, Vol. 2, 211-215, edited by R. L. Whistler and M. L. Wolfrom, Academic Press, New York, 1963, G. Hewit and G. Fletcher Jr., *ibid*, 226-228, and R. U. Lemieux, *ibid*, 223-224). The aglycon (Ra) is transferred to the monosaccharide by reacting a suitable thiol or alcohol, e.g. HSEt, HSPh, HOTMSEt, HO-allyl, or HOBn with the monosaccharide per-O-acylate using a Lewis acid such as boron trifluoride etherate (see e.g. R. J. Ferrier and R. H. Furneaux, *Carbohydr. Res.* 52 (1976), 63-68, J. Dahmén, T. Frejd, G. Grönberg, T. Lave, G. Magnusson, and G. Noori, *Carbohydr. Res.* 116 (1983), 303-307), or trimethylsilyl trifluoromethanesulfonate (see T. Ogawa, K. Beppu, S. Nakabayashi, *Carbohydr. Res.* 93 (1981), C6-C9) as promoters. The reaction is carried out in a suitable solvent such as chloroform, dichloromethane and/or toluene. When the monosaccharide derivative in question is a per-O-acylated glycosyl bromide or chloride, promoters such as silver trifluoromethanesulfonate or mercury(II) salts (see e.g. H. Paulsen, *Angew. Chem. Int. Ed. Engl.* 21 (1982), 155-173) can be used, and the reactions are carried out in suitable solvents such as dichloromethan and/or toluene. Th monosaccharide Ra-glycosides is obtained after de-O-acylation using sodium methoxide (see e.g. A. Thompson, M. L. Wolfrom, and E. Pascu,

Methods in Carbohydrate Chemistry, Vol. 2, 215-220, edited by R. L. Whistler and M. L. Wolfrom, Academic Press, New York, 1963) in methanol or in methanol containing a co-solvent such as dichloromethane or tetrahydrofuran.

In the second step (step 2) the monosaccharide Ra-glycoside is further derivatized. New functional groups (Rb) which will form part of the final product or act as protective groups during the subsequent glycosylation steps are introduced. Examples of functional group transformations are: OH-groups to ethers or esters (see e.g. *Protective Groups in Organic Synthesis* edited by T. W. Greene and P. G. M. Wuts, John Wiley & Sons, Inc., New York, 1991), OH-groups to carbonates (see e.g. J. March, *Advanced Organic Chemistry - Reaction Mechanisms, and Structure*, 347, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein), reductive removal or OH-groups via halides, sulfonates or other routes (see e.g. J. March, *Advanced Organic Chemistry - Reaction Mechanisms, and Structure*, 389-392, 394, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein, and H. H. Baer, *Pure Appl. Chem.* 61(7) (1989), 1217-1234, and references cited herein), OH-groups to halogen (see e.g. J. March, *Advanced Organic Chemistry - Reaction Mechanisms, and Structure*, 381-286, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein), OH-groups to azido groups (see e.g. J. March, *Advanced Organic Chemistry - Reaction Mechanisms, and Structure*, 380, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein, and H. H. Baer, *Pure Appl. Chem.* 61(7) (1989), 1217-1234, and references cited herein), OH-groups to amino groups via azides or other routes (see e.g. J. March, *Advanced Organic Chemistry - Reaction Mechanisms, and Structure*, 798-800. 1106, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein, and H. H. Baer, *Pure Appl. Chem.* 61(7) (1989), 1217-1234, and references cited herein), OH groups to keto groups (oxo) (see e.g. J. March, *Advanced Organic Chemistry - R action Mechanisms, and Structure*, 1048-1120, 3rd Ed., John Wiley & Sons, New York, 1985, and referenc s cited herein). OH groups to xomethylen derivatives via keto groups

r other r utes (see e.g. J. March, *Advanced Organic Ch mistry - R action M chanisms, and Structur* , 400-404, 407, 845-854, 3rd Ed., John Wiley & Sons, New York, 1985, and references cited herein), OH groups to alkyl groups via exomethylene derivatives and subsequent hydrogenation or via other routes (see e.g. H. O. H. House, *Modern Synthetic Reactions*, 1-130, 2nd Ed., W. A. Benjamin, Inc., Menlo Park, C.A., 1972, and references cites herein, or J. Yoshimura, *Adv. Carbohydr. Chem. Biochem.* 42 (1984), 69-134), and exchange of OH groups for heterocyclic groups via different routes (see e.g. A. R. Katrizky, *Handbook of Heterocyclic Chemistry*, Pergamon Press, Oxford, 1985).

In the third step (step 3), condensation of the Ra-glycosides substituted with functional groups (Rb) (protective groups known inn the art) from above are performed. For O-glycosidic linkages: One Ra-glycoside derivative is transformed to a glycosyl donor by activation at the anomeric centre, and reacted with another Ra-glycoside which has been transformed to a glycosyl acceptor by removing one or several protective groups (see e.g. H. Paulsen, *Angew. Chem. Int. Ed. Engl.* 21 (1982), 155-173, R. R. Schmidt, *Angew. Chem. Int. Ed. Engl.* 25 (1986), 212-235, P. Fügedi, P. J. Garegg, H. Lönn, and T. Norberg, *Glycoconj. J.* 4 (1987), 97-108, *Protective Groups in Organic Synthesis* edited by T. W. Greene and P G. M. Wuts, John Wiley & Sons, Inc., New York, 1991). For C-glycosidic linkages see e.g. R. R. Schmidt, and G. Effenberger, *Liebigs Ann. Chem.* (1987), 825-831, S. Czernecki, and G. Ville, *J. Org. Chem.* 54 (1989), 610-612, R. Preuss, and R. R. Schmidt, *J. Carbohydr. Chem.* 10(5) (1992), 887-900, O. Martin, and W. Lai, *J. Org. Chem.* 58 (1993), 176-185, or C. R. Bertozzi, P. D. Hoeprich, Jr., and M. D. Bednarski, *J. Org. Chem.* 57 (1992), 6092-6094. For S-glycosidic linkages see e.g. L-X Wang, N. Sakairi, and H. Kuzuhars, *J. Chem. Soc. Perkin Trans.* 1 (1990), 1677-1982, or M. Blanc-Meusser, L. Vigne, H. Driguez, J. Lehman, J. Streck, and K. Urbahns, *Carbohydr. R s.* 224 (1982), 59-71.

Further glycosidic linkages may be introduced by repeating the third st p.

In the fourth step (step 4) the substituent (R_c) at the reducing end is introduced. R_c is defined as $(Z_1-Z_{16})-R$, wherein R and Z_1-Z_{16} have the definition given for compounds Ia, Ib, Ic, Id, Ie and If. The term "$(Z_1-Z_{16})-R$" shall be read as Z_1-R, Z_2-R, Z_3-R..... $Z_{16}-R$. Activation of an oligosaccharide Ra-glycoside derivative from step 3 at the anomeric centre of the reducing end and reaction with a suitable nucleophile leads to O-, C-, S-, or N-glycosidic derivatives, respectively. A final product is obtained after removal of protective groups, if necessary. When the compound of the invention is in the form of a conjugate with a particular matrix, the Rc-glycoside derivative is further transformed via different routes to the final product (see e.g. Y. G. Lee, and R. T. Lee, *Glycoconjugates*, 121-164, edited by H. J. Allen, and E. C. Kisailus, Dekker, New York, 1992, R. Roy, F. D. Tropper, and A. Romanowska, *J. Soc., Chem. Commun.* (1992), 1611-1613, or C. P. Sotwell and Y. C. Lee, *Adv. Carbohydr. Chem. Biochem.*, Vol. 37 (1980), 225-281).

Copolymerisation reactions for preparation of copolymers of acrylamide and the mono-, di-, tri- or oligosaccharide glycosides with or without a spacer are performed by known methods, for example as described in E. Kallin, H. Lönn, T. Norberg and M. Elofsson, J. Carbohydr. Chemistry 8(4), 597-611 (1989) or M. Andersson and S. Oscarsson, Bioconjugate Chemistry, vol. 4(3), 246-247 (1993). The general strategy for preparation of these conjugates has been to attach an olefinic group to a carbohydrate, and then copolymerize this derivative with acrylamide. The olefinic group has been introduced into the carbohydrate molecule either as an allyl glycoside at an early stage by acryloylation of an amino function of a mono-, di-, tri- or oligosaccharide derivative or by other known methods.

As indicated above, pharmaceutical preparations containing the compounds of the general formula Ia, Ib, Ic, Id, Ie or If constitute a further aspect of the invention.

The compounds of the invention can be administered systemically or locally and are preferably administered orally or by injection, by the rectal route, by the transdermal route, by infusion or by inhalation in the form of a pharmaceutical preparation comprising the active ingredient in the form of the original compound or in the form of a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable carrier which may be a solid, semi-solid or liquid diluent or an ingestible capsule, and such preparations comprise a further aspect of the invention. Pharmaceutically acceptable carriers must, of course, be of sufficiently high purity and sufficiently low toxicity to render them suitable for administration to human or mammals being treated. The compounds may also be used without carrier material. As examples of pharmaceutical preparations may be mentioned tablets, capsules, dragees, solutions, drops, such as nasal drops, aerosols for inhalation, nasal spray, liposomes, etc. Usually the active substance will comprise between 0.01 and 99 % by weight of the preparation, e.g. between 0.5 and 20% by weight for preparations intended for injection and between 0.1 and 50% by weight for preparations intended for oral administration.

The preparations are preferably in unit dosage form, whether as single dosage units or as multiple dosage units.

To produce pharmaceutical preparations in the form of dosage units for oral application containing a compound of the invention, the active ingredient may be mixed with conventionally used solids, pulverulent carriers, e.g. lactose, saccharose, sorbitol, mannitol, a starch such as potato starch, corn starch, amylopectin, laminaria powder or citrus pulp powder, a cellulose derivative or gelatine and also may include lubricants such as magnesium or calcium stearate or a Carbowax

or other polyethylene glycol waxes and compressed to form tablets or cores for dragé s. If dragées are required, th cores may be coated with e.g. concentrated sugar solutions which may contain gum arabic, talc and/or titanium dioxide, or , alternatively, with a film forming agent dissolved in easily volatile organic solvents or mixtures of organic solvents. Dyestuffs can be added to these coatings, e.g. to distinguish between different contents of active substance. For the preparation of soft gelatine capsules consisting of gelatine and, e.g. glycerol and a plasticizer, or similar closed capsules, the active substance may be admixed with a Carbowax or a suitable oil such as e.g. sesame oil, olive oil, or arachis oil. Hard gelatine capsules may contain granulates f the active substance with solid, pulverulent carriers such as lactose, saccharose, sorbitol, mannitol, starches, e.g. potato starch or corn starch, or amylopectin, cellulose derivatives or gelatine, and may also include magnesium stearate or stearic acid as lubricants.

The compositions of the invention may be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the patient by employing procedures well known in the art.

By using several layers of the active drug, separated by slowly dissolving coatings, sustained release tablets are obtained. Another way of preparing sustained release tablets is to divide the dose of the active drug into granules with coatings of different thickness and compress the granules into tablets together with the carrier substance.

The active substance can also be incorporated in slowly dissolving tablets made of e.g. fat and wax substances or evenly distributed in a tablet of an insoluble substance such as a physiologically inert plastic substance.

Liquid pr parati ns f r oral application may be in th f rm of elixirs, syrups or suspensions, e.g. s luti ns c ntaining fr m

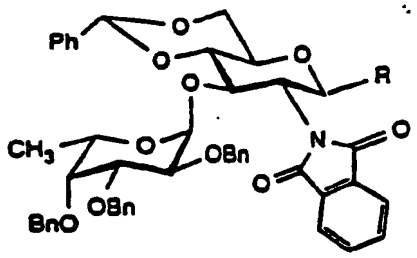
about 0.1% to 20% by weight of the active substance, sugar and a mixture of ethanol, water, glycerol, propyl ne glycol and optionally aroma, saccharin and/or carboxymethylcellulose as dispersing agents. The formulations can additionally include wetting agent, emulsifying and suspending agents, preserving agents and sweetening agents.

For parenteral application by injection, preparations may comprise an aqueous solution of the active drug or a physiologically acceptable salt thereof, desirably in a concentration of 0.5-20% and optionally also a stabilizing agent and/or buffer substances in aqueous solution. Dosage units of the solution may advantageously be enclosed in ampoules.

There is limited knowledge of compounds that inhibit the adherence of *Helicobacter pylori* to mucosal surfaces such that the compounds are useful in the prevention or treatment of gastrointestinal disorders and diseases caused or mediated by *Helicobacter pylori*. Because of this limited knowledge, the dosage at which the active ingredients may be administered may vary within a wide range and will depend on various factors such as e.g. the severity of the infection, the age of the patient etc. and may have to be individually adjusted.

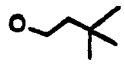
The pharmaceutical compositions of the subject invention preferably contain from about 1 mg to about 50 g, more preferably from about 10 mg to about 5 g per day of the active ingredient and may be divided into multiple doses.

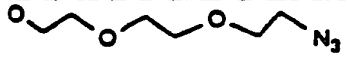
The invention is further illustrated by the following, non-limiting examples.

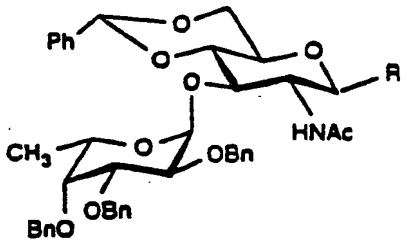


1 R = SEt

2 R = OMe

5 R = 

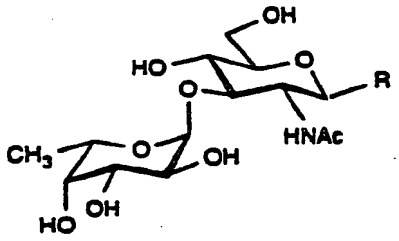
8 R = 



3 R = OMe

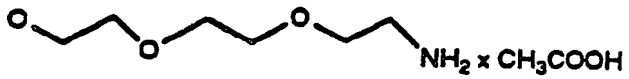
6 R = 

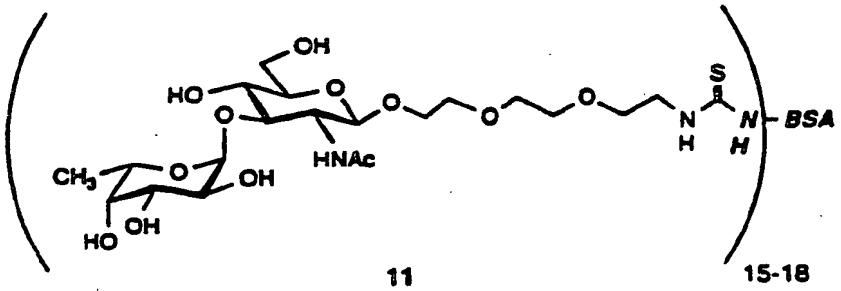
9 R = 



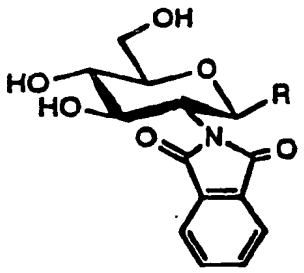
4 R = OMe

7 R = 

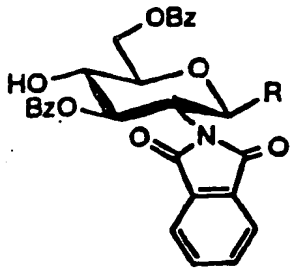
10 R = 



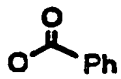
11 15-18

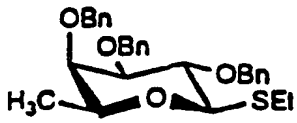


12 R = 



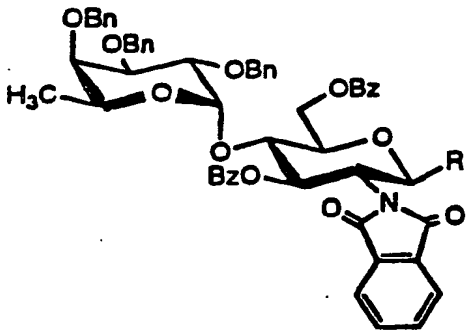
13 R = 

OBz = 

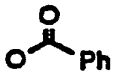


14

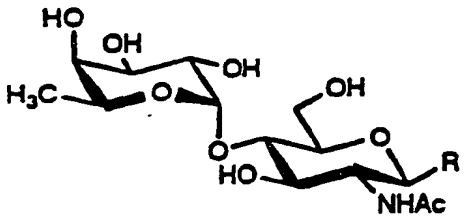
OBn = OCH_2Ph



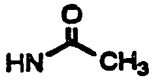
15 R = 

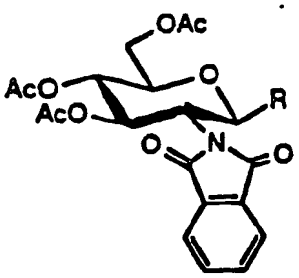
OBz = 

OBn = OCH_2Ph

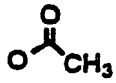


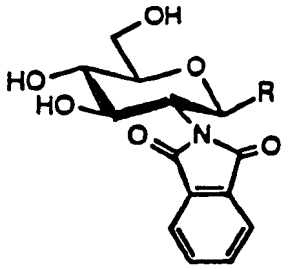
16 R = 

NHAc = 

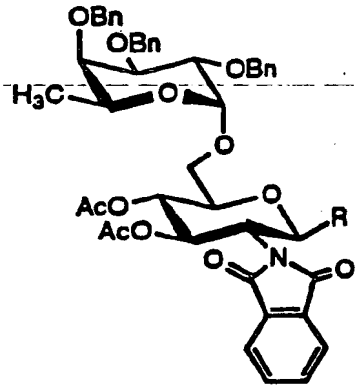


17 R = SEt

OAc = 



18 R = SEt

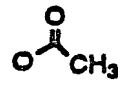


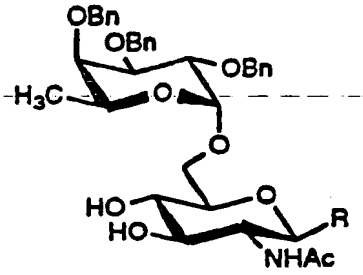
19 R = SEt

20 R = OMe

23 R = 

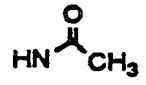
OBn = OCH_2Ph

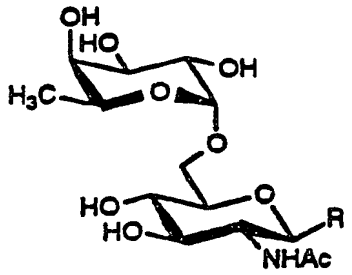
OAc = 



21 R = OMe

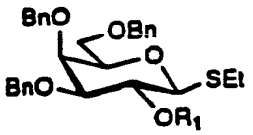
OBn = OCH_2Ph

NHAc = 



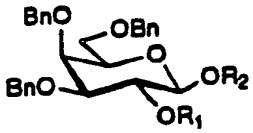
22 R = OMe

24 R = 



25 R_1 = Ac

26 R_1 = Bz

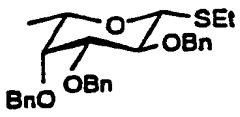


27 R_1 = Bz, R_2 = $-CH_2CH_2N_3$

28 R_1 = H, R_2 = $-CH_2CH_2N_3$

32 R_1 = Bz, R_2 = $-(CH_2CH_2O)_2CH_2CH_2N_3$

33 R_1 = H, R_2 = $-(CH_2CH_2O)_2CH_2CH_2N_3$



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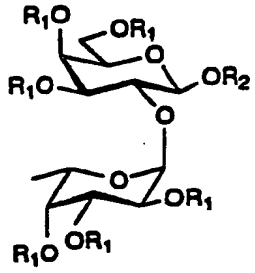


29 R_1 = Bn, R_2 = $-CH_2CH_2N_3$

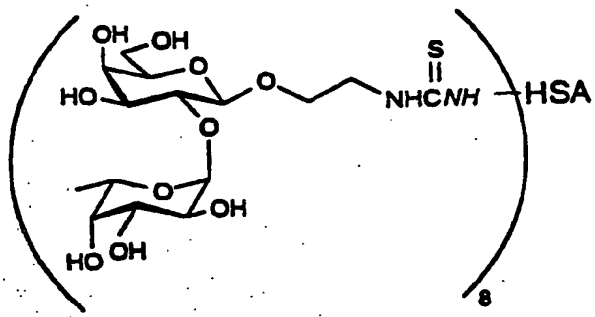
30 R_1 = H, R_2 = $-CH_2CH_2NH_2$

57 R_1 = H, R_2 = $-CH_2CH_2NHCOCH_2$

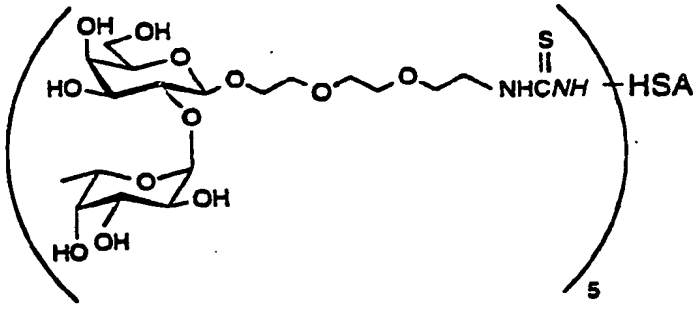
34 R_1 = Bn, R_2 = $-(CH_2CH_2O)_2CH_2CH_2N_3$

35 R_1 = H, R_2 = $-(CH_2CH_2O)_2CH_2CH_2NH_2$

37 R_1 = H, R_2 = $-(CH_2CH_2O)_2CH_2CH_2NHCOCHCH_2$



31



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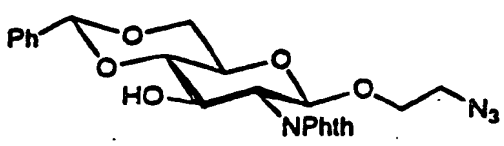

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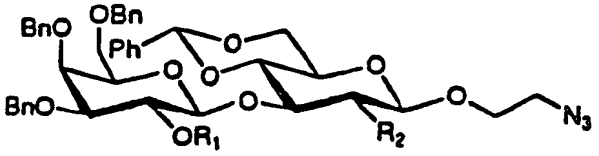
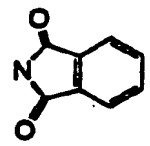
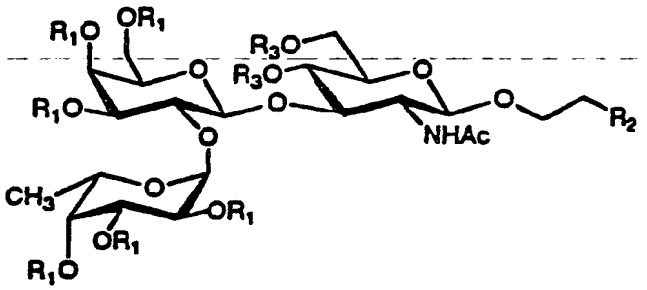


44 R_1 = Ac R_2 = NPhth

45 R_1 = OH R_2 = NHAc

NPhth =



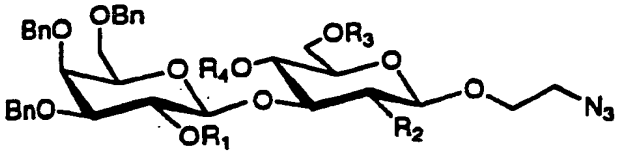


46 R_1 = Bn R_2 = N_3 R_3 = CHPh

47 R_1 = Bn R_2 = $NHCOCF_3$ R_3 = CHPh

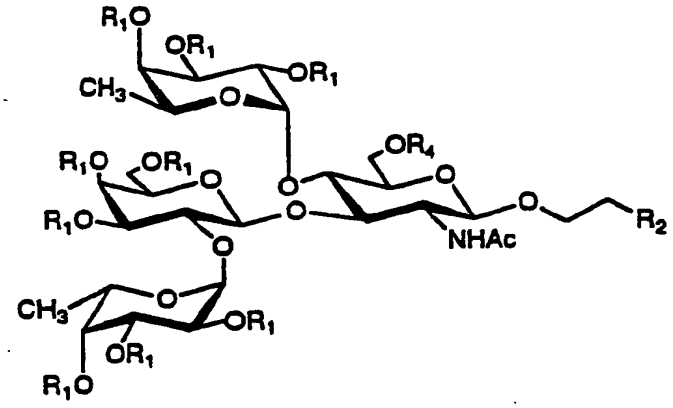
48 R_1 = H R_2 = $NHCOCF_3$ R_3 = H

49 R_1 = H R_2 = $NHCOCHCH_2$ R_3 = H



45 R_1 = H R_2 = NHAc R_3 , R_4 = CHPh

51 R_1 = H R_2 = NHAc R_4 = H R_3 = OBn

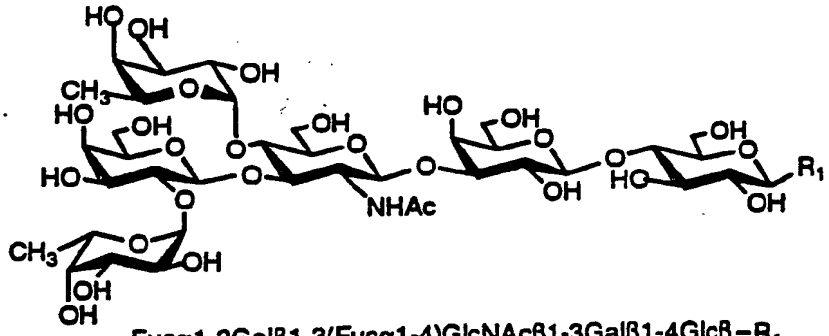


52 R_1 = Bn R_2 = N_3 R_4 = Bn

53 R_1 = Bn R_2 = $NHCOCF_3$ R_4 =Bn

54 R_1 = H R_2 = $NHCOCF_3$ R_4 = H

55 R_1 = H R_2 = $NHCOCH_2$ R_4 = H



Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ–R_1

39 R_1 = OH

40 R_1 = NH_2

41 R_1 = $NHCOCHCH_2$

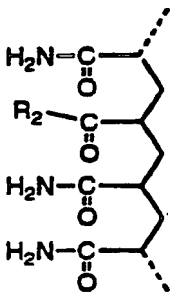
42 R_2 = Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1 -NH

38 R_2 = Fucα1-2Galβ1-$O(CH_2CH_2O)_2CH_2CH_2NH$

58 R_2 = Fucα1-2Galβ1-CH_2CH_2NH

50 R_2 = Fucα1-2Galβ1-3GlcNAcβ1-CH_2CH_2NH

56 R_2 = Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-CH_2CH_2NH



General methods

^1H and ^{13}C NMR spectra in examples 1 to 6 were recorded on a Varian Gemini 300 spectrometer and on a Varian Unity 400 MHz spectrometer. In examples 1 to 6 the following reference signals were used: $CHCl_3$, δ 7.25 (^1H in $CDCl_3$); $CHCl_3$, δ 77.9 (^{13}C in $CDCl_3$); $(CH_3)_2CO$, δ 2.24 or CHD_2OH δ 3.31 (^1H in D_2O); $(CH_3)_2CO$, δ 33.19 or CHD_2OH, δ 51.89 (^{13}C in D_2O); CHD_2OH, δ 3.31 (^1H in CD_3OD). ^1H and ^{13}C NMR spectra in all other examples were recorded at 25°C in $CDCl_3$ (using tetramethylsilane as internal standard for ^1H, $CDCl_3$ δ 77.0 for ^{13}C) and in D_2O (HDO δ 4.765 for ^1H, using aceton δ 30.0 as internal standard for ^{13}C). NMR spectra recorded for all compounds were in agreement with the structures postulated and only selected data are reported. Masspectra to determine the degree of substitution of carbohydrate component vs. protein were performed on a VG TOFSPEC linear time of flight masspectrometer. Fab-MS was run on a Nermag 1010L, with an Iontech FAB gun and a matrix of thioglycerol. Optical rotations were measured using a Perkin Elmer 241 polarimeter. Thin layer chromatography (TLC) was performed on Merck DC-Fertigplatten (Kiselgel 60 F254 0.25 mm) and spots were visualized by UV or by spraying with 10% sulphuric acid followed by charring at elevated temperature, or by spraying with phospohomolybdic acid or ninhydrin in n-butanol (0.5%). Silica gel 60 (40-63 λm) and Amicon Matrex® Silica Si 0.35-0.70 m was used for column chromatography.

Separations were also performed on a Chromatotron® rotary TLC using 1-2 mm layers of Silica Gel 60 PF_{254} with gipsum. All Biogel® P-2 column were eluated with 1% n-buthanol in deionized water if not otherwise stated.

EXAMPLE 1

Methyl 2-acetamido-2-deoxy-3-O-α-L-fucopyranosyl-β-D-glucopyranoside (4)

(i) Methyl 4,6-O-benzyliden -3-O-(tri-O-benzyl-α-L-fucopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (2)

Trifluoromethanesulfonic acid (2 μl, 0.023 mmol) was added to a stirred mixture of ethyl 3-O-(tri-O-benzyl-α-L-fucopyranosyl)-4,6-O-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (1) (100 mg, 0.117 mmol), (prepared according to H. Lönn, *Carbohydr. Res.* 139 (1985), 105-113) methanol (7 μl, 0.175 mmol), N-iodosuccinimide (40 mg, 0.175 mmol) and ground molecular sieves (100 mg, 3Å) in dichloromethane-diethyl ether (3 ml, 2:1) at -30°C. After 45 min the reaction mixture was filtered through a layer of Celite into an aqueous solution of sodium hydrogen carbonate and sodium bisulphite. The organic layer was separated, washed with aqueous sodium chloride, and concentrated. Column chromatography (toluene-ethyl acetate, 20:1) of the residue gave amorphous (2) (93 mg, 97 %), $[\alpha]_D$ -16.2° (c 1.0, $CHCl_3$).

^1H NMR data ($CDCl_3$, δ): 7.80 to 7.00 (24H, benzyl and phthaloyl), 5.29 (d, 1H, J 8.6 Hz, H-1), 4.84 to 4.25 (5H, CH_2Ph), 4.84 (bs, 1H, H-1'), 4.66 (dd, 1H, J 8.5 and 10.3 Hz, H-3), 4.48 to 4.43 (m, 1H, H-3'), 4.35 (dd, 1H, J 8.6 and 10.3 Hz, H-2), 4.08 (bdd, 1H, J 6.4 and 13.0 Hz, H-5'), 3.91 to 3.81 (2H), 3.78 to 3.66 (4H), 3.51 to 3.47 (1H), 3.48 (s, 3H, OCH_3), 0.90 (d, 3H, CH_3).

^{13}C NMR data ($CDCl_3$, δ): 168.0 (CO), 138.8 to 123.0 (benzyl), 101.1 (CHPh), 99.7 (C-1'), 99.4 (C-1), 82.1, 79.5, 78.0, 75.7, 75.5, 74.6, 73.0, 72.5, 68.6, 67.2 (C-5'), 66.1, 56.9 (OCH_3), 55.5 (C-2), 16.3 (CH_3).

(ii) Methyl 2-acetamido-3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (3)

A solution of (2) (1.13 g, 1.36 mmol) and hydrazine hydrate (3.3 ml, 68 mmol) in aqueous 95% ethanol was boiled under

reflux for 20 h, cooled, and concentrated. The residu was acetylated with acetic anhydride-pyridine (50 ml, 1:1) overnight. The solution was concentrated, and the residue was subjected to column chromatography (heptane-ethyl acetate, 1:1) to give crude (3) which was used directly in the next step.

^{1}H NMR data ($CDCl_3$, δ): 7.50 to 7.25 (20H, benzyl), 5.71 (d, 1H, J 7.4, NH), 5.52 (s, 1H, CH_2Ph), 5.09 (d, 1H, H-1'), 4.85 to 4.58 (6H, CH_2Ph), 4.82 (d, 1H, H-1), 4.37)dd, 1H, J 4.6 and 10.4 Hz, H-6), 4.28 (bt, 1H, H-3), 4.12 to 4.05 (2H, H-2' and H-5'), 3.95 (dd, 1H, J 2.6 and 10.2 Hz, H-3'), 3.78 (bt, 1H, H-6), 3.63 (bs, 1H, H-4'=, 3.60 (bt, 1H, H-4), 3.53 (m, 1H, H-5), 3.48 (s, 3H, OCH_3), 3.42 (ddd, 1H, J 7.2, 8.2 and 9.5 Hz, H-2), 1.67 (s, 3H, NHAc), 0.84 (d, 3H, CH_3).

^{13}C NMR data ($CDCl_3$, δ): 170.6 (CO), 138.6 to 126.2 (benzyl), 101.8 (C-1), 101.6 (CHPh), 98.4 (C-1'), 80.8 (C-4), 79.8 (C-3'), 77.6 (C-4'), 77.0 (C-2' or C-5'), 75.1 (C-3), 74.9 (CH_2Ph), 72.5 (CH_2Ph), 68.8 (C-6), 66.9 (C-2' or C-5'), 66.2 (C-5), 58.1 (C-2), 57.0 (OCH_3), 23.2 (NHAc), 16.3 (CH_3).

(iii) Methyl 2-acetamido-2-deoxy-3-O-α-L-fucopyranosyl-β-D-glucopyranoside (4)

A solution of crude (3) (1.05 g) in acetic acid-ethyl acetate-water (9:5:1, 120 ml) was hydrogenolysed at 200 kPa over 10% Pd/C (1 g) over night. The mixture was filtered through a layer of Celite and concentrated. Column chromatography (chloroform-methanol-water, 65:35:6) of the residue gave amorphous 4 (469 mg, 90% calculated from (2), $[\alpha]_D$ -116.0° (c 1.0, water).

^{1}H NMR data (D_2O, acetone ref., δ): 4.99 (d, 1H, J 4.0 Hz, H-1'), 4.46 (d, 1H, J 8.7 Hz, H-1), 4.33 (bdd, 1H, H-5'), 3.98 to 3.45 (9H), 3.51 (s, 3H, OCH_3), 2.03 (s, 3H, NHAc), 1.17)d, 3H, CH_3).

^{13}C NMR data (D_2O, acetone ref., δ): 177.6 (CO), 104.7 (C-1), 102.9 (C-1'), 83.5, 78.8, 74.7, 72.5, 71.6, 70.9, 69.9, 63.7, 60.0, 59.1 (C-2), 25.2 (NHAc), 18.1 (CH_3).

EXAMPLE 2

3,3-Dimethylbutyl 2-acetamido-2-deoxy-3-O-α-L-fucopyranosyl-β-D-glucopyranoside (7)

(i) 3,3-Dimethylbutyl 3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (5)

Trifluoromethanesulfonic acid (30 µl, 0.35 mmol) was added to a stirred mixture of (1), 3,3-dimethyl-butan-1-ol (317 µl, 2.62 mmol), N-iodosuccinimide (602 mg, 2.62 mmol), and ground molecular sieves (1.5 g, 3Å) in dichloromethane-diethyl ether (2:1, 45 ml) at -30°C. After 45 min the reaction mixture was filtered through a layer of Celite into an aqueous solution of sodium hydrogen carbonate and sodium bisulphite. The organic layer was separated, washed with aqueous sodium chloride, and concentrated. Column chromatography (heptane-ethyl acetate, 6:1) of the residue gave amorphous (5) (1.42 g, 90%), $[\alpha]_D$ -22.2° (c 1.0, $CHCl_3$).

^1H NMR data ($CDCl_3$, δ): 7.80 to 7.0 (24 H, benzyl and phthaloyl), 5.57 (s, 1H, CHPh), 5.35 (d, 1H, J 8.5 Hz, H-1), 4.84 (bs, 1H, H-1'), 4.83 to 4.24 (5H, CH_2Ph), 4.65 (dd, 1H, J 8.3 and 10 3 Hz, H-3), 4.34 (dd, 1H, J 8.5 and 10.4 Hz, H-2), 4.07 (dd, 1H, J 5.5 and 10.4 Hz, H-5'), 3.96 to 3.66 (7 H, inter alia OCH_2), 3.53 to 3.45 (2H, inter alia OCH_2), 1.46 to 1.29 (m, 2H, $CH_2C(CH_3)_3$), 0.88 (d, 3H, J 6.4 Hz, CH_3), 0.73 (s, 9H, $CH_2C(CH_3)_3$).

^{13}C NMR data ($CDCl_3$, δ): 168.0 (CO), 138.8 to 123.0 (benzyl and phthaloyl), 101.1 (CHPh), 99.4 (C-1'), 98.9 (C-1), 82.1, 79.5, 76.0, 75.7 (C-3), 75.6, 74.6, 73.0, 72.6, 68.7, 67.3 (OCH_2),

67.2 (C-5), 66.2, 55.8 (C-2), 42.4 ($CH_2C(CH_3)_3$), 30.8 ($CH_2C(CH_3)_3$), 29.4 ($CH_2C(CH_3)_3$), 16.3 (CH_3).

(ii) 3,3-Dimethylbutyl 3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (6)

A solution of (5) (1.42 g, 1.58 mmol) and hydrazine hydrate (3.9 ml, 79 mmol) in aqueous 90% ethanol (100 ml) was boiled under reflux for 20 h, cooled, and concentrated. The residue was acetylated with acetic anhydride-pyridine (50 ml, 1:1) overnight. The solution was concentrated. Column chromatography (heptane-ethyl acetate, 3:1, containing 1% methanol) of the residue gave amorphous (6) (1.16 g, 90%), $[\alpha]_D$ -74.7° (c 1.0, $CHCl_3$).

^1H NMR data ($CDCl_3$, δ): 7.50 to 7.20 (20 H, benzyl), 5.63 (d, 1H, J 7.3 Hz, NH), 5.51 (s, 1H, CH_2Ph), 5.07 (d, 1H, J 3.1 Hz, H-1'). 4.93 to 4.57 (6H, CH_2Ph), 4.92 (d, 1H, H-1), 4.39 to 4.29 (2H, H-6 and H-3), 4.11 to 4.04 (2H, H-2'and H-5'), 3.98 to 3.85 (2H, H-3'and OCH_2), 3.77 (bt, 1H, H-6), 3.61 (bs, 1H, H-4'), 3.55 (bt, 1H, H-4), 3.59 to 3.44 (2H, H-5 and OCH_2), 3.33 (bdd, 1H, H-2), 1.63 (s, 3H, OAc), 1.56 to 1.40 (m, 2H, $CH_2C(CH_3)_3$), 0.89 (s, 9H, $CH_2C(CH_3)_3$), 0.82 (d, 3H, CH_3).

^{13}C NMR data ($CDCl_3$, δ): 170.4 (CO), 138.6 to 126.0 (benzyl), 101.6 (CHPh), 100.7 (C-1), 98.1 (C-1'), 80.9 (C-4), 79.8 (C-3'), 77.6 (C-4'), 77.0 (C-2'or C-5'), 74.9 (C-3), 74.8 (CH_2Ph), 74.0 (CH_2Ph), 72.5 (CH_2Ph), 68.9 (OCH_2 or H-6), 67.5 (OCH_2 or H-6), 66.8 (C-5' or C-2'), 66.2 (C-5), 58.6 (C-2), 42.7 ($CH_2C(CH_3)_3$), 29.7 ($CH_2C(CH_3)_3$), 29.6 ($C(CH_3)_3$), 23.2 (NHAc), 16.2 (CH_3).

(iii) 3,3-Dimethylbutyl 2-acetamido-2-deoxy-3-O-α-L-fucopyranosyl-β-D-glucopyranoside (7)

A solution of th compound (6) (1.08 g, 1.33 mm l) in acetic acid:ethyl acetate:water, 9:5:1 (120mL) was hydrogenolysed at

200 kPa over 10% Palladium on charcoal (Pd/C) (1 g) over night. The mixture was filtered through a layer of Celite and concentrated. Column chromatography (chloroform-methanol-water, 100:30:3) of the residue gave amorphous (7) (566 mg, 94%), $[\alpha]_D$ -109-7° (c 1.0, water).

^1H NMR data (D_2O, acetone ref., δ): 4.99 (d, 1H, H-1'), 4.84 (s, 1H, CHPh), 4.34 (bdd, 1H, H-5'), 4.02 to 3.43 (11H), 2.01 (s, 3H, NHAc), 1.57 ti 1.41 (m, 2H, $CH_2C(CH_3)_3$), 1.17 (d 3H, CH_3), 0.90 (s, 9H, $C(CH_3)_3$).

^{13}C NMR data (D_2O, acetone ref., δ): 177.3 (CO), 103.6 (C-1), 102.8 (C-1'), 83.6, 78.8, 74.8, 72.5, 71.6, 70.9, 69.8, 63.7, 58.1 (C-2), 44.9 ($CHC(CH_3)_3$), 31.9 ($C(CH_3)_3$), 31.9)$C(CH_3)_3$), 25.2 (NHAc), 18.1 (CH_3).

EXAMPLE 3

Fucα1-3GlcNAcβ1-O-Spacer 1-BSA-conjugate (11)

(i) 8-Azido-3,6-dioxaoctyl 3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (8)

Trifluoromethanesulfonic acid (24 µl, 0.27 mmol) was added to a stirred mixture of (1) (1.15 g, 1.34 mmol), 8-azido-3,6-dioxaoctan-1-ol (352 µl, 2.01 mmol) (prepared according to P. H. Amvam-Zollo and P. Sinaï, *Carbohydr. Res.* 150 (1986), 199-212), N-iodosuccinimide (461 mg, 2.01 mmol) and ground molecular sieves (1.15 g, 3Å) in dichloromethane-diethyl ether (30 ml, 2:1) at -30°C. After 1 h the reaction mixture was filtered through a layer of Celite into a aqueous solution of sodium hydrogen carbonate and sodium bisulphite. The organic layer was separated, washed with aqueous sodium chloride, and concentrated. Column chromatography (heptane-ethyl acetate, 2:1) of the residue gave amorphous (8) (1.03 g, 79%), [α]D -21-7° (c 1.0, $CHCl_3$).

^{1}H NMR data ($CDCl_3$, δ): 7.80 to 7.05 (24H, Bzl, Phth), 5.59 (s, 1H, CHPh), 5.44 (d, 1H, J 8.6 Hz, H-1), 4.83 (bs, 1H, H-1'), 4.83 to 4.24 (5H, CH_2Ph), 4.65 (dd, 1H, J 8.5 and 10.3 Hz, H-3), 4.45 to 4.41 (1H, H-3'), 4.39 (dd, 1H, J 8.6 and 10.3 Hz, H-2), 4.09 (dd, 1H, J 6.4 and 12.6 Hz, H-5'), 3.99 to 3.83 (3H, inter alia OCH_2), 3.81 to 3.68 (5H, inter alia OCH_2), 3.61 to 3.30 (11H, inter alia OCH_2 and CH_2N_3), 0.90 (d, 3H, J 6.4 Hz, CH_3).

^{13}C NMR data ($CDCl_3$, δ): 169.0 (CO), 138.9 to 123.1 (Bzl, Phth), 101.1 (CH_2Ph), 99.4 (C-1'), 98.9 (C-1), 82.1, 79.6, 78.0, 75.6, 75.5, 74.7, 73.1, 72.6, 70.5, 70.4, 70.1, 69.9, 69.1, 68.7, 67.2, 66.2, 55.7 (C-2), 50.6 (CH_2N_3), 16.4 (CH_3).

(ii) 8-Azido-3,6-dioxaoctyl 2-acetamido-3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (9)

A solution of (8) (633 mg, 0.65 mmol) and hydrazine hydrate (1.6 ml, 33 mmol) in aqueous 90% ethanol (45 ml) was boiled under reflux for 24 h, cooled, and concentrated. The residue was acetylated with acetic anhydride-pyridine (50 ml, 1:1) overnight. The solution was concentrated. Column chromatography (chloroform-acetone, 9:1) and re-chromatography (ethyl acetate-heptane, 3:1) of the residue gave amorphous (9) (440 mg, 77%), $[\alpha]_D$ -72.6° (c 1.0, $CHCl_3$).

^{1}H NMR data ($CDCl_3$, δ): 7.50 to 7.25 (20H, benzyl), 7.92 (d, 1H, J 5.9 Hz, NH), 5.51 (s, 1H, CHPh), 5.16 (d, 1H, J 3.5 Hz, H-1'), 4.93 (d, 1H, J 7.7, H-1), 4.95 to 4,56 (6H, CH_2Ph), 4.34 (dd, 1H, J 4.9 and 10,4 Hz, H-6), 4.26 (bt, 1H, H-3), 4.12 (bdd, 1H, H-5'), 4.06 (dd, 1H, J 3.5 and 10.1 Hz, H-2'), 3.95 (dd, 1H, J 2.7 and 10.1 Hz, H-3'), 3.90 (bt, 1H, H-6), 3.81 to 3.45 (14H, inter alia OCH_2), 3.40 (m, 2H, CH_2N_3), 1.74 (s, 3H, NHAc), 0.84 (d, 3H, J 6.4 Hz, CH_3).

^{13}C NMR data ($CDCl_3$, δ): 170.4 (CO), 138.7 to 126.1 (benzyl), 101.5 (CHPh), 101.2 (C-1), 97.8 (C-1'), 80.6 (C-4), 79.6

(C-3'), 77.7 (C-4'), 76.7 (C-2' or C-5'), 74.9 (C-3), 74.6 (CH_2Ph), 73.7 (CH_2Ph), 72.2 (CH_2Ph), 70.6 (CH_2O), 70.6 (CH_2O), 70.4 (CH2O), 69.9 (CH_2O), 68.8 (CH_2O), 68.8 (H-6), 66.7 (C-2' or C-5'), 66.2 (C-5), 57.8 (C-2), 50.6 (CH_2N_3), 23.2 (NHAc), 16.2 (CH_3).

(iii) 8-Amino-3,6-dioxaoctyl 2-acetamido-2-deoxy-3-O-α-L-fucopyranosyl-β-D-glucopyranoside acetic acid salt (10)

A solution of (9) (57 mg, 0.065 mmol) in acetic acid-water (9:1, 30 ml) was hydrogenolysed at 200 kPa over 10% Pd/C (100 mg) over night. The mixture was filtered through a layer of Celite and concentrated. The residue was first subjected to column chromatography on silica gel (chloroform-methanol-water, 4:4:1) and then on Al_2O_3 (Merck, basic, 0.063-0.200 mm, chloroform-methanol-water, 4:4:1) to give amorphous (10) (18 mg, 51%), $[\alpha]_D$ -70.6° (c 0.2, water).

^{1}H NMR data (D_2O, acetone ref., δ): 4.98 (d, 1H, J 4.0 Hz, H-1'). 4.53 (d, 1H, J 8.6 Hz, H-1). 4.32 (bdd, 1H, H-5'), 4.05 to 3.42 (19H), 3.19 (m, 2H, CH_2NH_2), 2.01 (s, 3H, NHAc), 1.88 (CH_3COOH), 1.14 (d, 3H, J 6.6 Hz, CH_3).

^{13}C NMR data (D_2O, acetone ref., δ): 184.2 (CH_3COOH), 103.8 (C-1), 102.8 (C-1'), 83.3, 78.8, 74.8, 72.6, 72.5 72.4, 72.0, 71.5, 70.9, 69.8, 69.4, 63.7, 58.1 (C-2), 42.0 (CH_2NH_2), 26.3 (CH_3COOH), 25.2 (NHAc), 18.1 (CH_3).

(iv) Fucα1-3GlcNAcβ1-O-Spacer 1-BSA-conjugate (11)

Thiophosgene (67 µl, 0.856 mmol) in acetone (6 ml) was added dropwise to an ice-cold solution of (10) (120 mg, 0.214 mmol) in water-ethanol-0.1 M phosphate buffer pH 7 (1:1:1, 30 ml). The pH was kept at 6-7 with aqueous sodium hydroxide (1 M) during the reaction. After 20 min the mixture was extracted with diethyl ether (30 ml), concentrated to a volume of 10 ml, and added to a solution of bovin serum albumin (695 mg, 10.7 mmol) in aqueous sodium hydrog n carb nate (15 ml, 0.1 M, pH

9.3). During the addition, pH was adjusted to 9 with aqu ous sodium hydroxid (1 M). After 24 h the reaction mixture was desalted by ultrafiltration (Filtron, omegacell 150, 10 K) and freeze-dried to give (11) (672 mg). The degree of substitution was determined by sugar analysis (see M. A. Jermyn, *Anal. Chem.* 68 (1975), 332-335) to 15-18 mol disaccharide/mol protein.

EXAMPLE 4

2-Trimethylsilylethyl 2-acetamido-2-deoxy-4-O-α-L-fuco-pyranosyl-β-D-glucopyranoside (16)

(i) Trimethylsilylethyl 3,6-di-O-benzoyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (13)

2-Trimethylsilylethyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (12) (1.64 g, 4.0 mmol) (prepared as described by K. Jansson, S. Ahlfors, T. Frejd, J. Kilhberg, G. Magnusson, J. Dahmén, G. Noori, and K. Stenvall, *J. Org. Chem.* 53 (1988), 5629-5647), was dissolved in pyridine-dichloromethane (3:1, 24 ml) and cooled to -45°C. A mixture of benzoyl chloride (1060 ml, 9.1 mmol) and pyridine (900 ml) was added during 30 minutes. The reaction was completed after 3 hours and methanol (40 ml) was added. The solvents were evaporated and the residue was co-evaporated with toluene 3 times. The residue was chromatographed (SiO_2, heptane/ethyl acetate 2:1→1:1) to give pure (13) (2.38 g, 96%). $[\alpha]_D^{20}$ +69.4° (c 1.2, $CHCl_3$).

^1H NMR data ($CDCl_3$, δ): d 7.3-8.2 (m, 14H, 2 O-benzyl, N-phthalamoyl), 5.88 (dd 1H, J 7.1, 8.3 Hz, H-3), 5.46 (d, 1H, J 8.5 Hz, H-1), 4.79 (dABq, 1H, J 4.2, 12.4 Hz, H-6), 4.67 (dABq, 1H, J 1.9, 11.7 Hz, H-6), 4.45 (dd, 1H, J 8.4, 10.8 Hz, H-2), 3.8-4.1 (m, 3H, H-4, H-5, OCH_2CH_2), 3.57 (dt, 1H, J 7.2, 9.7 Hz, OCH_2CH_2), 0.7-1.0 (m, 2H, CH_2Si), -0.15 (s, 6H, $SiMe_3$).

(ii) 2-Trimethylsilylethyl 3,6-di-O-benzoyl-4-O-(2,3,4-tri-O-b nzyl-α-L-fuc pyran syl)-2-deoxy-2-phthalimid -β-D-glucopyranoside (15)

Compound (13) was dissolved in dichloromethane-N,N-dimethylformamide (8 ml, 5:3) and tetrabutylammonium bromide (664 mg, 2.06 mmol) and molecular sieves (4 Å, 4 g, activated) was added. To a solution of thioethyl 2,3,4-tri-O-benzyl-1-thio-β-L-fucopyranoside (14) (986 mg, 2.06 mmol) (prepared according to H. Lönn, *Carbohydr. Res.* 139 (1985), 105-113) in dichloromethane (8 ml) was added bromine (122 ml, 2.37 mmol) in dichloromethane (2 ml). After 15 min stirring, cyclohexene (distilled) was added dropwise until the bromine colour disappeared. This solution was then added to the mixture abov containing compound (13) and stirred for 48 h. The mixture was then filtered through Celite, the solvents were evaporated and the residue was co-concentrated with toluene three times. Column chromatography of the residue (heptane/ethyl acetate, 5:1→ 1:1) gave (15) (896 mg, 85%), $[\alpha]D^{20}$ + 14.6° (c 1.2, $CHCl_3$).

^1H NMR data ($CDCl_3$, δ): 5.44 (d, 1H, J 8.5 Hz, H-1), 4.80 (d, 1H, J 3.6 Hz, H-1').

(iii) 2-Trimethylsilylethyl 2-acetamido-2-deoxy-4-O-(α-L-fucopyranosyl)-β-D-glucopyranoside (16)

Compound (15) (760 mg, 0.74 mmol) was dissolved in methanol (7 ml) and sodium methoxide (220 ml, 2 M in methanol) was added. The solution was stirred over night at room temperature and then neutralized with Amberlite IR-120(H). Filtration and evaporation of the solvents gave a syrup. The syrup was dissolved in acetic acid (15 ml) and 10% Pd/C (860 mg) was added. After 1.5 h hydrogenolysis (100 kPa), the mixture was filtered and the solvents evaporated. The resulting syrup was dissolved in ethanol (18 ml) and hydrazine hydrate was added. The solution was refluxed for 3 h. Evaporation of the solvents and co-evaporation with ethanol 5 times gave a syrup that was dissolved in methanol-water mixture (5:1, 60 ml). Acetic anhydride (5 ml) was added and the s lution was stirred for 1.5 h. The s lvents were evaporated. C lumn chr matography (SiO_2,

dichloromethane/methanol, 5:1) gave (16) (100 mg, 29%), $[\alpha]_D^{20}$ -113.5° (c 0.7, H_2O).

^1H NMR data (D_2O, δ): d 4.93 (d, 1H, J 3.66 Hz, H-1'), 4.52 (d, 1H, J 8.06 Hz, H-1).

EXAMPLE 5

Methyl 2-acetamido-2-deoxy-6-O-α-L-fucopyranosyl-β-D-glucopyranoside (22)

(i) Ethyl 2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (18)

Ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (17) (5.79 g, 12 mmol) (prepared according to H. Lönn, *Carbohydr. Res.* (1985) **139**, 105-113) was dissolved in methanol (250 ml) and methanolic sodium methoxide (0.2 M, 2.5 ml) was added. The mixture was stirred for 15 h. Neutralization with acidic cation exchange resin (Bio-Rad AG® 50W-X8), filtration, evaporation and crystallization from water gave (18) (3.83 g, 89%), m.p. approx. 96°C; m.p. after recrystallization 159-161°C; $[\alpha]_D^{22}$ +9.8° (c 0.9, methanol).

^1H NMR data (CD_3OD, CHD_2OD ref., δ) d: 7.91-7.79 (5H), 5.32 (d, 1H, J 10.5 Hz, H-1), 4.28 (dd, 1H, J 10 and 8 Hz, H-3), 4.05 (t, 1H, J 10.5 Hz, H-2), 3.93 (dd, 1H, J 12 and 2 Hz, H-6), 3.73 (dd, 1H, J 12 and 5.5 Hz, H-6), 3.46 (ddd, 1H, J 10, 5.5 and 2 Hz, H-5), 3.40 (dd, 1H, J 10 and 8 Hz, H-4), 2.74 (dq, 1H, J 12.5 and 7.5 Hz, SCH), 2.63 (dq, 1H, J 12.5 and 7.5 Hz, SCH) and 1.17 (t, 3H, J 7.5 Hz, CH_3CH_2).

(ii) Ethyl 3,4-di-O-acetyl-6-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (19)

Bromine (0.485 ml, 9.4 mmol) was added to a solution of ethyl 2,3,4-tri-O-benzyl-1-thi -β-L-fucopyran side (14) (4.5 g, 9.4 mmol) in dichloromethane (70 ml) at 0°C. The mixture was

stirred for 35 min and was then evap rated twice with benzene. Cyclohexene (0.5 ml) was added and the mixture was again evaporated with benzene. The residue was dissolved in dichloromethane (25 ml) and then added during 1 h, to a stirred mixture of compound (18) (3.32 g, 9.4 mmol), powdered molecular sieves (20 g, 4 Å) and tetraethylammonium bromide (3.5 g) in dimethylformamide (75 ml). The reaction mixture was stirred for 2 h at 0°C, then for 2 h at room temperature followed by filtering through Celite. The filtrate was partitioned between dichloromethane and saturated aqueous sodium hydrogen carbonate. The aqueous phase was extracted with dichloromethane and the combined organic phases were washed with water, and concentrated. The residue was chromatographed (ethyl acetate-heptane; 1:1→3:1) to give a crude product, which was O-acetylated by stirring in acetic anhydride (50 ml) and pyridine (75 ml) for 17 h at room temperature. Evaporation with toluene and chromatography (ethyl acetate-heptane; 1:2→1:3) gave (19) (3.3 g, 40%), $[\alpha]_D^{22}$ -4.6° (c 1.4, chloroform).

^{1}H-NMR data ($CHCl_3$, δ): 7.90-7.83 (2H), 7.79-7.71 (2H), 7.45-7.24 (15H), 5.83 (dd, 1H, J 10 and 9.5 Hz, H-3), 5.43 (d, 1H, J 10.5 Hz, H-1), 5.09 (dd, 1H, J 10 and 9.5 Hz, H-4), 4.99 and 4.67 (2H, AB-system, J 11.5 Hz, benzylic H), 4.97 (d, 1H, J 3.5 Hz, H-1'), 4.89 and 4.77 (2H, AB-system, J 12 Hz, benzylic H), 4.79 and 4.73 (2H, AB-system, J 12 Hz, benzylic H), 4.39 (t, 1H, J 10.5 Hz), 4.06 (dd, 1H, J 10 and 3.5 Hz), 3.97-3.87 (3H), 3.76 (dd, 1H, J 12 and 6 Hz), 3.70- 3.62 (2H), 2.67 (dq, 1H, J 12 and 7.5 Hz, SCH), 2.56 (dq, 1H, J 12 and 7.5 Hz, SCH), 1.98 (s, 3H, CH_3CO), 1.87 (s, 3H, CH_3CO), 1.15 (t, 3H, J 7.5 Hz, CH_3CH_2), 1.13 (d, 3H, J 7.5 Hz, Fuc-CH_3).

Calc. for $C_{47}H_{51}NO_{12}S$: C 66.1; H 6.02; N 1.64; S 3.75. Found: C 66.4; H 6.1; N 1.55; S 3.25.

(iii) Methyl 3,4-di-O-acetyl-6-O-(2,3,4-tri--O-benzyl-α-L-fucopyranosyl)-2-deoxy-2-phthalimido-β-D-gluc pyranoside (20)

To a mixture of (19) (853 mg, 1 mmol), methanol (0.102 ml, 2.5 mmol), N-iodosuccinimide (344 mg, 1.52 mg) and ground molecular sieves (0.9 g, 4 Å) in dichloromethan -diethyl ether (2:1, 25 ml) at -30°C, was added trifluoromethanesulphonic acid (0.030 ml, 0.3 mmol). After 2.5 h. the reaction mixture was filtered through Celite into an aqueous solution of sodium hydrogen carbonate and aqueous sodium bisulphite. The organic phase was separated and washed with saturated aqueous sodium chloride, and concentrated. Chromatography (ethyl acetate- heptane; 2:3) of the residue gave (20) (778 mg, 94%), $[\alpha]_D^{22}$ -2.8° (c 1.1, chloroform).

^{1}H NMR data ($CHCl_3$, δ): 7.90-7.82 (2H), 7.78-7.70 (2H), 7.45-7.24 (15H), 5.79 (dd, 1H, J 11 and 9 Hz, H-3), 5.26 (d, 1H, J 8.5 Hz, H-1), 5.08 (dd, 1H, J 10 and 9 Hz, H-4), 4.99 and 4.67 (AB-system, 2H, J 11.5 Hz, benzylic H), 4.96 (d, 1H, J 3.5 Hz, H-1'), 4.88 and 4.77 (AB-system, 2H, J 12 Hz, benzylic H), 4.81 and 4.69 (AB system, 2H, J=12 Hz, benzylic H), 4.28 (dd, 1H, J 11 and 8.5 Hz, H-2), 4.07 (dd, 1H, J 10 and 3.5 Hz), 3.99-3.85 (3H), 3.77 (dd, 1H, J 12 and 6 Hz), 3.71-3.64 (2H), 3.34 (s, 3H, CH_3O), 2.00 (s, 3H, CH_3CO), 1.86 (s, 3H, CH_3CO), 1.14 (d, 3H, J 6.5 Hz, Fuc-CH_3).

Calc. for $C_{46}H_{49}NO_{13}$: C 67.06; H 5.99; N 1.70. Found: C 67.0; H 6.1; N 1.65.

(iv) Methyl 2-acetamido-6-O-(2,3,4-tri-O-benzyl-α-L--fucopyranosyl)-2-deoxy-β-D-glucopyranoside (21)

Compound(20) was deacetylated in methanolic sodium methoxide (9.5 mM, 31.5 ml) for 1.5 h. Neutralization with acidic cation exchange resin (Bio-Rad AG® 50W-X8), filtration and concentration gave a residue which was dissolved in methanol (20 ml). Hydrazine monohydrate (0.8 ml) was added and the mixture was heated under reflux for 4 h and then cooled to 10°C. Water (15 ml) and ac tic anhydride (5 ml) were added and the r action mixture was stirred at room temperatur . Aft r 20 min a white precipitate was obtained. Additi n f methan l (10

ml) facilitated stirring. After additional 2.5 h, pyridine (2 ml) was added which resulted in a clear solution. The mixture was then stirred for 30 min. The methanol was evaporated and the aqueous residue was extracted with dichloromethane. The organic phase was washed with 1 M HCl and saturated aqueous sodium hydrogen carbonate, and concentrated. Chromatography (ethyl acetate-methanol, 10:1) of the residue gave (21) (435 mg, 77%). An analytical sample was crystallized from ethanol, m.p. 224-226°C (d), $[\alpha]_D^{22}$ -75.4° (c 0.9, $CHCl_3$).

^1H NMR data ($CDCl_3$-CD_3OD, 3:1, CHD_2OD ref., δ) d: 7.41-7.20 (15H), 4.91 and 4.61 (AB-system, 2H, J 11.5 Hz, benzylic H), 4.80 and 4.70 (AB-system, 2H, J 11.5 Hz, benzylic H), 4.78 (d, 1H, J 3 Hz, H-1'), 4.75 (s, 2H, benzylic H), 4.24 (d, 1H, J 8.5 Hz, H-1), 4.09-3.97 (2H), 3.92 (dd, 1H, J 10 and 2.5 Hz), 3.86 (dd, 1H, J 11 and 2 Hz), 3.77-3.56 (3H), 3.42 (dd, 1H, J 9.5 and 8.5 Hz) 3.36 (s, 3H, CH_3O), 1.97 (s, 3H, CH_3CO), 1.07 (d, 3H, J 6.5 Hz, Fuc-CH_3).

(v) Methyl 2-acetamido-2-deoxy-6-O-α-L-fucopyranosyl-β-D-glucopyranoside (22)

A solution of (21) (362 mg, 0.56 mmol) in acetic acid (50 ml) was hydrogenolysed at 230 kPa over 10% Pd/C (160 mg) over night. The mixture was filtered through a layer of Celite and concentrated. Column chromatography (chloroform-methanol-water, 65:40:10) of the residue gave amorphous (22) (192 mg, 90%,), $[\alpha]_D^{22}$ -106° (c 1.1, H_2O).

^1H NMR data (D_2O, CH_3OH ref., δ) : 4.95 (d, 1H, J 4 Hz, H-1'), 4.46 (d, 1H, J 8.5 Hz, H-1), 4.15 (q, 1H, J 6.5 Hz), 4.02 (dd, 1H, J 12 and 1.5 Hz), 3.92 (dd, 1H, J 10.5 and 3.5 Hz), 3.84-3.67 (4H), 3.62-3.49 (6H), 3.51 (s, CH_3O), 1.24 (d, 3H, J 6.5 Hz, Fuc-CH_3).

^{13}C NMR data (D_2O, CH_3OH ref., δ) : 177.7, 105.0, 102.4, 78.0, 76.9, 74.8, 72.9, 72.5, 71.2, 70.3, 69.7, 60.0, 58.5, 25.2, 18.3.

EXAMPLE 6

3,3-Dimethylbutyl 2-acetamido-2-deoxy-6-O-α-L-fucopyranosyl-β-D-glucopyranoside (24)

(i) 3,3-Dimethylbutyl 3,4-di-O-acetyl-6-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (23)

To a stirred mixture of (19) (853 mg, 1 mmol), 3,3 dimethylbutan-1-ol (0.182 ml, 1.5 mmol), N-iodosuccinimide (344 mg, 1.52 mmol) and powdered molecular sieves (0.9 g, 4 Å) in dichloromethane-diethyl ether (2:1; 25 ml) at -30°C, was added trifluoromethanesulphonic acid (0.017 ml, 0.19 mmol). After 1 h additional 3,3-dimethylbutan-1-ol (0.100 ml, 0.82 mmol) and trifluoromethanesulphonic acid (0.015 ml, 0.17 mmol) were added and stirring was continued for 2.5 h. The reaction mixture was then filtered through Celite into an aqueous solution of sodium hydrogen carbonate and sodium bisulphite. The organic phase was washed with aqueous sodium chloride and concentrated. The residue was submitted to chromatography (ethyl acetate-heptane; 2:5) to give (23) (740 mg, 83%), $[\alpha]_D^{22}$ -8.5° (c 1.3, $CHCl_3$).

^1H NMR data ($CHCl_3$, δ): 7.89-7.82 (2H), 7.78-7.70 (2H), 7.44-7.24 (15 H), 5.79 (dd, 1H, J 11 and 9 Hz, H-3), 5.32 (d, 1H, J 8.5 Hz, H-1), 5.08 (dd, 1H, J 10 and 9 Hz, H-4), 4.99 and 4.66 (AB-system, 2H, J 11.5 Hz, benzylic H), 4.91 (d, 1H, J 3.5 Hz, H-1'), 4.88 and 4.77 (AB-system, 2H, J 12 Hz, benzylic H), 4.80 and 4.69 (AB system, 2H, J=12 Hz, benzylic H), 4.29 (dd, 1H, J 11 and 8.5 Hz, H-2), 4.05 (dd, 1H, J 10 and 3.5 Hz), 3.99-3.73 (6H), 3.70-3.63 (2H), 3.38 (m, 1H), 1.98, (s, 3H, CH_3CO), 1.87 (s, 3H, CH_3CO), 1.30 (m, 2H, OCH_2CH_2), 1.13 (d, 3H, J 6.5 Hz, Fuc-CH3), 0.69 (s, 9H).

Calc. for $C_{51}H_{49}NO_{13}$: C 69.3; H 5.59; N 1.59. Found: C 68.4; H 6.65; N 1.75.

(ii) 3,3-Dimethylbutyl 2-acetamido-2-deoxy-6-O-α-L-fucopyranosyl-β-D-glucopyranoside (24)

Compound (23) (680 mg, 76 mmol) was dissolved in methanol (25 ml). Methanolic sodium methoxide (0.2 M, 1 ml) was added and the mixture was stirred for 3.5 h. Neutralization with acidic cation exchange resin (Bio-Rad AG® 50W-X8), filtration and evaporation gave a residue which was dissolved in methanol (20 ml). Hydrazine monohydrate (0.5 ml, 10.3 mmol) was added and the mixture was heated under reflux for 3.5 h and then cooled to 10°C. Water (10 ml), methanol (2 ml) and acetic acid anhydride (2.5 ml) were added and the mixture was stirred at room temperature for 2.5 h during which time additional portions of acetic acid anhydride (2.0 and 0.5 ml) were added. The methanol was then evaporated, and the aqueous residue was partitioned between dichloromethane and water. The aqueous phase was extracted with dichloromethane and the organic phase was concentrated. Chromatography of the residue (ethyl acetate-methanol; 20:1) gave a product which was dissolved in acetic acid (50 ml). 10% Pd/C (160 mg) was added and the mixture was hydrogenolyzed at 230 kPa for 4 h at room temperature. The mixture was filtered through a layer of Celite and concentrated. Column chromatography of the residue (chloroform-methanol-water, 150:40:3→65:40:10) of the residue gave amorphous (24) (275 mg, 80%,), $[\alpha]_D^{22}$ -87.2° (c 0.95, H_2O).

^1H NMR data (D_2O, CH_3OH ref., δ) : 4.94 (d, 1H, J 4 Hz, H-1'), 4.54 (d, 1H, J 8.5 Hz, H-1), 4.15 (q, 1H, J 6.5 Hz), 4.03-3.88 (8H), 2.03 (s, 3H, CH_3CON), 1.58-1.40 (2H, OCH_2CH_2), 1.24 (d, 3H, J 6.5 Hz, Fuc-CH_3), 0.90 (s, 9H).

^{13}C NMR data (D_2O, CH_3OH ref., δ) : 177.5, 104.0, 102.4, 77.9, 76.9, 74.9, 73.0, 72.6, 71.2, 71.0, 69.7, 58.6, 45.0, 31.9, 25.2, 18.4.

Calc. for $C_{20}H_{37}NO_{10}$: C 53.2; H 8.26; N 3.10. Found: C 51.2; H 8.25; N 3.2.

EXAMPLE 7

Fucα1-2Galβ1-O-spacer 4-HSA (31)

i) Ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (25)

Compound (25) was prepared from acetobromogalactose (70.73 g, 0.172 mmol), according to proceedure described by S Nilsson, H Lönn and T Norberg, Glycoconjugate J., 1989, 6, 21-34. Yield of (25) was 26.13 g (28%).
TLC: Rf 0.33 (heptane:ethyl acetate, 9:2)

^{13}C-NMR ($CDCl_3$) δ: 170.2 (CO), 139.2, 138.6, 138.4 (aromatic C), 84.2, 82.1 78.1, 75.0, 74.1, 73.6, 72.6, 70.3, 69.2, (C-1,2,3,4,5,6, 3x CH_2Ph), 24.1 (SCH_2CH_3), 21.6 ($OCOCH_3$), 15.4 (SCH_2CH_3).

^1H-NMR ($CDCl_3$) δ: 5.43 (bt, 1H, $J_{2,3}$ 9.7 Hz, H-2), (d 1H, $J_{1,2}$ 11.9 Hz, H-1), 4.01 (bd, 1H, $J_{3,4}$ 2.9 Hz, H-4), 3.55 (dd, 1H, H-3).

(ii) Ethyl 2-O-benzoyl-3,4,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (26)

Ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (25) was deacetylated with sodium methoxide in methanol (50 ml, pH 12) and subsequently benzoylated with benzoylchloride (1.96 gr., 14 mmol) in pyridine (20 ml) according to standard procedures. Crystalline 26 was obtained in almost quantitative yield (3.44 gr., 97%).

NMR ($CDCl_3$) ^1H: δ 5.70 (1H, t, 9.8Hz, H-2) 2.60-2.80 (2H, m, -CH_2CH_3),

^{13}C: δ 14.8, 23.6 (SEt), 68.6, 70.2, 71.7, 72.8, 73.6, 74.4, 76.6, 127.5-138.6 (aromatic C), 165.4 (C=O)

(iii) 2-Azidoethyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (28)

To a stirred suspension of the thioglycoside (26) (700 mg, 1.17 mmol), 2-azidoethanol (204 mg, 2.34 mmol; prepared according to A. Ya. Chernyak et al. and A.V. Rama Rao, Carbohydr. Res., 1992, 223, 303-309), N-iodosuccinimide (395 mg, 1.75 mmol,) and ground molecular sieves (3Å, 400 mg) in dichloromethane (25 ml) was added at 0°C trifluoromethanesulfonic acid (TfOH; 35 mg, 0.23 mmol; according to method published by G.H. Veeneman, S.H. Van Leeuwen, J.H. Van Boom, Tetrahedron Lett., 1990, 31, 1331). When TLC (toluene:ethyl acetate, 6:1) showed complete conversion (< 15 minutes), reaction was quenched by addition of triethylamine at 0°C. The solution was filtered through a layer of celite, diluted with dichloromethane and washed twice with aqueous $Na_2S_2O_3$ (10%) and finally with water. The organic phase was dried over magnesium sulfate, filtered and concentrated and the residue was immediately subjected to TLC (toluene:ethyl acetate, 15:1). Solvent removal left 672 mg of 2-Azidoethyl 2-O-benzoyl-3,4,6-tri-O-benzyl-β-D-galactopyranoside (27) as a colourless oil (92%), which was treated with sodium methoxide in methanol (pH 11) at room temperature for 6 hours. The solution was neutralized with Dowex 50 H^+ resin, filtered and concentrated. The crystalline product (28) (540 mg, 89% from 2) was used without further purification for the preparation of disaccaride (29).

Compound (27): NMR ($CDCl_3$) ^1H: δ5.66 (1H, dd, 10.0, 7.9 HZ, H-2) 4.57 (1H, d, 7.8 Hz, H-1)
^{13}C: δ 50.7 (CH_2N_3, 67.3, 68.7, 71.9, 72.5, 73.6, 73.9, 74.5, 101.4 (C-1), 127.6-137.8 (aromatic C), 165.3 (C=O)

C mpound (28): ^{13}C: δ 50.7 (CH_2N_3), 68.4, 68.7, 71.4, 72.6, 73.0, 73.6, 73.9, 74.5, 81.7, 103.4 (C-1), 125.3-138.4 (aromatic C)

(iv) 2-Azid ethyl 3,4,6-tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (29)

To a solution of thioethylglycoside (14) (400 mg, 0.836 mmol) in dichloromethane (10 ml), bromine (134 mg, 0.836 mmol) was added at 0°C. After about 5 minutes at 0°C, the solution was allowed to attain room temperature and the solvent was evaporated. After co-evaporation with toluene the residue was dissolved in dichloromethane (2 ml) and added at room temperature to a suspension of tetraethylammonium bromide (176 mg, 0.836 mmol; prepared according to R.U. Lemieux, K.B. Hendriks, R.V. Stick, K. James, J. Am. Chem. Soc. 1975, 97:14, 4056), compound (28) (290 mg, 0.558 mmol) and ground molecular sieves (3Å, 300 mg) in CH_2Cl_2:DMF (4:1, 7 ml). TLC (toluene:ethyl acetate, 6:1) showed complete conversion after stirring for 20 hours. The mixture was filtered, diluted with dichloromethane and washed with water. The organic phase was dried over magnesium sulfate and filtered and concentrated in vacuo. Preparative TLC yielded the title compound (29) as a viscous oil (407 mg, 78%).

NMR ($CDCl_3$) ^{13}C: δ 16.5, 33.6, 50.9, 66.4, 66.9, 68.8, 71.4, 72.0, 72.8, 72.9, 73.5, 73.6, 74.4, 74.8, 75.7, 78.1, 79.6, 84.3, 97.3, 102.0, 125.3-129.0 (aromatic C), 138.0, 138.3, 139.0.

(v) 2-Aminoethyl 2-O-α-L-fucopyranosyl-β-D-galactopyranoside (30)

The protected disaccaride derivative (29) (80 mg, 85 μmol) was dissolved in ethanol (abs., 10 ml) and water (1 ml) and Pd/C (10%, 100 mg) was added. The mixture was hydrogenated and stirred rapidly at room temperature at 50 PSI. When reaction was not completed within 60 hours, the mixture was filtered and the product formed was isolated (TLC, ethyl acetate:methanol:acetic acid:water, 5:3:3:1, R_f=0.15). After concentration in vacuo, the residue was resolved in a buffer of aqueous pyridine/acetic acid (2.5%/1%, pH 5.4) and eluated

through a Bi Gel P-2 column. Evaporation and freeze drying gave 14 mg (44%) of the title compound (30) as a white powder.

NMR ($CDCl_3$) ^{13}C: δ 16.8, 39.8, 61.1, 66.4, 67.1, 68.7, 69.6, 71.9, 73.0, 75.0, 78.4, 100.0, 101.7

(vi) Fucα1-2Galβ1-O-spacer 4-HSA (31)

To a stirred ice-cooled solution of thiophosgene (10 eq.) in tetrahydrofuran (2 ml), the amino derivative (30) (30 μmol) in sodium borate buffer (0.85 M, 2 ml, pH 8.5) was added. The solution was stirred at room temperature for 10 minutes and then extracted with diethylether (3 x 2 ml). The aqueous phase containing the isothiocyanate derivative was added to a solution of Human Serum Albumine (HSA) (1/30 eq.) in the same buffer system (0.5 ml). pH was adjusted to 8.5 with aqueous sodium hydroxide (0.25 M) and the mixture was stirred at room temperature for 48 hours. Freeze drying of the reaction mixture was followed by ultracentrifugation purification with Centriprep tubes (10KO). Freeze drying of the purified solutions gave the HSA-conjugates (31) in excellent yield (18 mg).The degree of substitution was determined by Time of Flight masspectroscopy to 8 mol disaccharide/mol protein.

EXAMPLE 8

Fucα1-2Galβ1-O-spacer 1-HSA (36)

(i) 8-Azido-3,6-dioxaoctyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (33)

The azidoderivative (33) was synthesized from the thioglycoside (26) (1004 mg, 1.68 mmol) and 1-azido-8-hydroxy-3,6-dioxaoctane (686 mg, 3.35 mmol; prepared according to C.R. Bertozzi, M.D. Bednarski, J. Org. Chem., 1991, 56, 4326-4329) according to a procedure similar to the one used for synthesis of derivative (28) (TLC; toluene:EtOAc 6:1) showed complete conversion within 40 minutes. Similar workup and deacylation f 8-azido-3,6-

dioxaoctyl 2-O-benzoyl-3,4,6-tri-O-benzyl-β-D-galactopyranoside (32) yielded 933 mg (78% from 26) of the title compound (33) as a viscous oil.

Compound (32); NMR ($CDCl_3$): ^1H: δ 5.64 (1H, dd, 10.0, 7.9 Hz, H-2).
^{13}C: δ 50.6 (CH_2N_3), 68.7, 68.9, 69.8, 70.3, 70.5, 70.7, 71.8, 71.9, 72.6, 73.6, 73.8, 74.6, 80.0, 101.6 (C-1)

Compound (33); ^{13}C: δ 50.6 (CH_2N_3), 68.7, 68.8, 70.0, 70.2, 70.5, 70.6, 71.4, 72.6, 73.3, 73.5, 73.8, 74.5, 81.9, 103.8 (C-1)

(ii) 8-Azido-3,6-dioxaoctyl 3,4,6-tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (34)

Disaccaride (34) was synthesized from compound (33) (500 mg, 0.82 mmol) and thioethylglycoside (14) (512 mg, 1.07 mmol) according to the procedure described for the corresponding derivative (29). Preparative TLC gave 683 mg (81%) of the title compound (34) as an oil.

NMR ($CDCl_3$) ^{13}C: δ 18.3, 50.2, 66.2, 68.2, 68.8, 70.0, 70.2, 70.3, 70.6, 71.2, 72.0, 72.3, 72.5, 73.0, 73.3, 73.6, 74.4, 74,6, 75.8, 78.0, 79.7, 84.2, 98.6, 102.0

(iii) 8-Amino-3,6-dioxaoctyl 2-O-α-L-fucopyranosyl-β-D-galactopyranoside (35)

8-Azido-3,6-dioxaoctyl 3,4,6-tri-O-benzyl-2-O-(2,3,4 tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (34) (35 mg, 34 μmol) was dissolved in a mixture of ethyl acetate:ethanol:water in 1:2:2 (vol., 12 ml) and acidified with 20 μl HOAc (according to method published by S. Nilsson, Doctoral dissertation, Lund University, April 1992). The solution was hydrogenated at 50 PSI on 10% Pd/C (140 mg) at room temperature overnight and when TLC (thyl ac tate:m than 1:acetic acid:water, 5:3:3:1) showed complete deprotection, the mixture

was filtered and evaporated. Purification on a Bio-Gel P-2 column (aq. pyridine:acetic acid, 2.5:1 by vol., pH 5.4) concentration and freeze drying gave the title compound (35) as a white powder (14 mg, 90%).

NMR ($CDCl_3$) ^{13}C: δ 15.2 (CH_3), 38.9, 60.7, 66.1, 66.5, 68.1, 68.5, 68.7, 69.2, 69.3, 69.4, 69.6, 71.7, 73.4, 74.8, 76.6, 99.2 (C-1^{Pr}), 101.4 (C-1).

(iv) Fucα1-2Galβ1-O-spacer 1-HSA (36)

To a stirred ice-cooled solution of thiophosgene (10 eq.) in tetrahydrofuran (2 ml), the amino derivative (35) (30 μmol) in sodium borate buffer (0.85 M, 2 ml, pH 8.5) was added. The solution was stirred at room temperature for 10 minutes and then extracted with diethylether (3 x 2 ml). The aqueous phase containing the isothiocyanate derivative was added to a solution of Human Serum Albumine (HSA) (1/30 eq.) in the same buffer system (0.5 ml). pH was adjusted to 8.5 with aqueous sodium hydroxide (0.25 M) and the mixture was stirred at room temperature for 48 hours. Freeze drying of the reaction mixture was followed by ultracentrifugation purification with Centriprep tubes (10KO). Freeze drying of the purified solutions gave the HSA-conjugates 36 in excellent yields (33 mg).
The degree of substitution was determined by Time of Flight masspectroscopy to 5 mol disaccharide/mol protein.

EXAMPLE 9

Fucα1-2Galβ1-O-spacer 2-PAA (38)

(i) 8-N-acrylamido-3.6-dioxaoctyl 2-O-α-L-fucopyranosyl-β-D-galactopyranoside (37)

0.8 ml deaerated 0.5 M sodiumborate aq. buffer (pH 8.5) and 2.4 ml deaerated methanol was added to 15 mg of the compound (35). The reaction mixture was flush d with nitr gen and c oled to

0°C. 3.3 μl of acryloylchloride was added and stirring was continued for 10 minutes. The reaction mixture was concentrated at room temperature to about a third of its original volume. Purification on a Bio-Gel® P2 column and lyophilization gave the title compound (37) (14 mg, 83%)

NMR-data: ^{13}C (D_2O): δ 15.0 (CH_3), 38.54 (CH_2N), 60.51, 66.31, 67.87, 68.19, 68.30, 68.50, 68.98, 69.10, 69.12, 69.43, 71.50, 73.25, 74.55, 76.08 (C-2,3,4,5,6; C-2,3,4,5; 5xCH_2O) 98.88 (C-1'), 101.16 (C-1), 126.92 and 129.43 ($CH=CH_2$).

(ii) Fucα1-2Galβ1-O-spacer 2-PAA (38)
To a solution of the compound (37) (14 mg, 0.027 mmol) and acrylamide (9.7 mg, 0,14 mmol) in deaerated water (1 ml) was added first N,N,N'N'-tetramethylendiamine (6 μl) and then ammonium persulphate (3.5 mg). The mixture was stirred at roomtemperature over night. The polymer (38) obtained was purified by gel chromatography on a Bio-Gel® P2 column. Freeze-drying of the purified solutions gave the PAA conjugate in excellent yield (17.9 mg). ^1H-NMR showed an average incorporation of 1 oligosaccharide per 7 acrylamide units.

EXAMPLE 10

Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ-3Galβ1-4Glcβ1-NH-PAA (42)

(i) Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-NH_2 (40). Solid ammonium bicarbonate was added until saturation to a solution of Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glc1-OH (Lewis B hexasackaride (39), purchased from Iso Sep AB, 25 mg in water (1.25 mL). The mixture was stirred in an open vessel at room temperature for 6 days. Ammonium bicarbonate was added at intervals, saturation was assured by always keeping a portion of solid salt present in the mixture. When TLC indicated no more c nversi n, the mixture was diluted with water (5 mL) and concentrated t half th original volum . The residue was diluted to 20 mL with water and concentrated to 5 mL. This process was repeated once, then the residue was

diluted to 10 mL and lyophilized. The crude product was put n a Bio-gel P2-column, and the fraction containing Lewis B glycosylamine (40) was collected, (20 mg 80%).

NMR data: ^{13}C (D_2O): δ 84.66 (C-NH_2), 97.54, 99.33, 100.39, 100.72, 102.98 (C-1 carbons of the nonreducing sugarunits), 15.08, 15.13 (2xCH_3-fucose), 21.95 (CH_3-CON-GlcNAc).

(ii) Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-NH-CO-CH=CH_2 (41)

Sodium carbonate (50 mg) and deaerated methanol (0.5 mL) was added to a solution of the glycosylamine (40) (20 mg, 0.02 mmol) in water (0.5 mL). The mixture was stirred at 0°C while acryloyl chloride (60 μL., 0.74 mmol) in tetrahydrofuran (0.5 mL) was added during 5 min. After 10 min. the solution was diluted with water (3 mL) and concentrated to 2 mL. The solution was again diluted with water (2 mL), 200 μL tetrahydrofuran (inhibitor solution) was added, and the solution was concentrated to 1-2 mL. This solution was purified by gel filtration on a Bio-Gel® P2 column. Appropriate fractions were pooled and lyophilized to obtain the title compound (41) (14 mg, 67%).

NMR data: ^{13}C (D_2O): δ 81.28 (C-NHCOCHCH_2), 97.42, 99.18, 100.25, 102.59, 102.85 (C-1 carbons of the nonreducing sugarunits), 14.99, 15.06 (2xCH_3-fucose), 21.92 (CH_3CON-GlcNAc), 125.93, 130.32,(CH=CH_2).
Fab ms: pseudomolecular ion m/z; 1053 (M+H) and 1075 $(M+Na)^+$.

(iii) Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ-3Galβ1-4Glcβ1-NH-PAA (42)

Copolymerization of N-Acryloylglycosylamine with acrylamide. A solution of the N-acryloylglycosylamine (41) (13 μmol) and acrylamide (53 μmol, 3.7 mg) in distilled water (200 μL) was deaerated by flushing with nitrogen for 20 min. The solution was then stirred at 0°C and N,N,N,',N'-tetramethylethylenediamine (2 μL) and ammonium persulfate (1

mg) were add d. The mixture was slowly stirred at 0°C for 2 hours and then at room temperature vernight. The viscous solution was diluted with water (1 mL) and purified by gel filtration on Bio-Gel® P2 column eluated with aqueous n-buthanol (1%). Fractions containing polymer were pooled and lyophilized. Yield: 3mg.

^{1}H-NMR shows presence of approximately 1 Lewis-B unit per 5 $CHCH_2$ units.

EXAMPLE 11

Fucα1-2Galβ1-3GLcNAcβ1-O-Spacer 5-PAA (50)

(i) 2-azidoethyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (43)

Ethyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (prepared according to H Lönn, Carbohydr. Res., 139 (1985), 105-113) (0.5 g, 1.1 mmol) was dissolved in 20 ml of dichloromethane and 2-azidoethanol (prepared according to Chernyak A.Y. et al. Carbohydr. Res., 1992, 223, (303-309) (0.148 g, 1.7 mmol) crushed 4Å molecular sieves were added and the mixture stirred for 30 min. Dimethyl(methylthio)sulfonium triflate (DMTST) (0.439 g, 1.7 mmol; prepared according to P. Fügedi and P.J. Garegg, Carbohydr. Res., 149 (1989), 9-12) was added at room temperature and stirring was continued for 4 hours. Analysis by TLC (toluene-ethylacetate) show no starting material, and to the reaction mixture was added 1 ml of triethylamine and stirring was continued for another 30 min. The reaction mixture was transfered to a silica gel column and eluted with toluene:ethylacetate 6:1 to give (372 mg, 72%) of the title compound (43).

NMR-data: ^{13}C ($CDCl_3$): δ 50.38 (CH_2-N); 56.42 (CH-N); 66.2, (CH-O); 68.44 (CH_2O); 68.50 (CH-O; 68.53 (CH_2-O); 82.05 (CH-O); 98,89 (C-1); 101.83 (PhCH).

(ii) 2-Azidoethyl 3-O-(2-O-acetyl-3,4,6-tri-O-benzyl-β-D-galcatopyranosyl)-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (44)

Ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (25) (818 mg, 1.5 mmol) and the compound (43) (395 mg, 0.85 mmol) were dissolved in 30 ml of dichloromethan , crushed 4Å molecular sieves were added and the mixture stirred for 20 min. The reaction was flushed with nitrogen and DMTST (787 mg, 3.05 mmol, dissolved in 5 ml of dichloromethane) was added dropwise to the reaction mixture and the dropfunnel rinsed with 6 ml of dichloromethane. After 2 hours 1 ml of triethylamine was added and stirred for 30 min., filtration, concentration and column chromatography (toluene:ethylacetate 10:1 gave three fractions. Fraction 1 the α-product (97.32, 98.89; (C-1 and C-1'). Fraction 2 almost pure 44 (306 mg, 39%).

NMR-data: ^{13}C ($CDCl_3$ ref. tetramethylsilane 0 ppm): δ 20.32 (CH_3CO), 50.47 (CH_2N), 55.13 (CH-N), 66.57, 68.15, 68.20, 68.65, 71.58, 71.71, 72.17, 72.94, 73.46, 74.38, 75.15, 80.47, 81.08 (C-3,4,5,6 C-2,3,4,5,6; 3xCH_2Ph; CH_2-O), 98.86 (C-1), 100.75, 101.23 (C-1 and CH Ph), 168.84 (C=O).

(iii) 2-azidoethyl 2-acetamido-3-O-(3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosid (45)

To compound (44) (525 mg, 0.56 mmol) was added 50 ml of ethanol and 1.1 ml of hydrazinhydrate reflux over night and TLC (toluene:ethylacetate 1:2) showed a new product. Concentration and coevaporation with toluene, followed and then dissolving in 45 ml of dichloromethane and washing with an equal amount of water, coevaporation with toluene, gave the crude monohydroxy amine. This crude product was dissolved in dichloromethane:methanol (1:1, 15 ml) and 1.5 ml of acetic anhydride was added. After 3 hours no starting material was left (TLC). Concentration and chr mat graphy (toluene-

ethylacetate 1:2) gave (204 mg, 45%) of the titl compound (45).

NMR-data: ^{13}C ($CDCl_3$): δ 23.59 ($NHCOCH_3$), 50.59 (C-N), 56.89 (C-N), 66.40, 68.28, 68.56, 70.55, 72.44, 73.21, 73.40, 73.53, 74.60, 76.08, 79.75, 81.71 (C-3,4,5,6; C-2',3',4',5',6'; 3xCH_2Ph; CH_2O) 100.97, 101.25, 103.48 (C-1, C-1^1 and CHPh), 171.67 (C=O).

(iv) 2-azidoethyl 2-acetamido-3-O-(3,4,6-tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galctopyranosyl]-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (46)

The compound (45) (137 mg, 0.17 mmol) and the compound (14) (162 mg, 0.34 mmol) were dissolved in dichloromethane (75 ml), and molecular sieves (4Å) were added, and the mixture was stirred for 20 min. DMTST (96 mg, 0.37 mmol) was added and stirring was continued for 1.5 hours. 1 ml of triethylamine was added and stirring was continued for another 20 min. Filtration through celite, concentration and column chromatography (toluene:ethylacetate 1:1) gave (46) (101 mg, 49%).

NMR-data: ^{13}C ($CDCl_3$): δ 16.83 (CH_3 fucose), 23.30 ($NHCOCH_3$), 50.66 (CH_2-N), 57.40 (C-2), 66.55, 67.17, 67.96, 68.60, 72.31, 72.91, 72.99, 73.04, 73,10, 73.51, 74.48, 74.65, 76.05, 76.29, 76.62, 77.60, 79.43, 79.53, 83.21 (C-3,4,5,6; C-2',3',4',5',6'; C-2", 3",4",5"; 6xCH_2Ph), 97.67 (C-1"), 100.94, 101.07, 102.13 (C-1, C-1', CHPh), 170.92 (C=O).

(v) 2-trifluoracetamidoethyl 2-acetamido-3-O-[3,4,6-tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (47).

The compound (46) (135 mg, 0.11 mmol) was dissolved in 11 mL of ethanol and 10% Pd/C (140 mg) was added. The reaction mixture was hydrogenated at atmospheric pressure for 15 minutes. Analysis by Tlc (ethyl acetate:methanol:acetic acid:water

12:3:3:1) showed no starting material, but one ninhydrin positive pr duct. The mixture was filtered through celite, concentrated and dissolved in dichloromethane (7 mL), and pyridine (3.5 mL), flushed with nitrogen and cooled to 0°C. Trifluoroacetic anhydride (31 µl, 0.22 mmol) was added. After one hour the mixture was concentrated and coevaporated with 2 ml of toluene twice. Column chromatography (toluene:ethyl acetate, 1:3) gave 47 (73 mg, 52%)

NMR-data: ^{13}C ($CDCl_3$): δ 17.06 (CH_3 fucose) 22.66 ($NHCOCH_3$), 39.59 (CH_2-N), 54.83 (C-2), 65.56, 66.77, 67.78, 68.44, 68.69, 72.80, 73.05, 73.24, 2x73.46, 74.46, 74.66, 76.38, 77.08, 77.80, 78.91, 79.96, 80.01, 82.07, (C-3,4,5,6; C-2',3',4',5',6'; C-2",3",4",5"; 6xCH_2Ph) 98.61 (C-1"), 101.22, 101.99, 102.35 (C-1, C-1', CHPh), 171.64 ($NHCOCH_3$).

(vi) 2-trifluoroacetamidoethyl 2-acetamido-2-deoxy-3-O-[2-O-(α-L-fucopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (48)

Trisaccharide (47) (73mg, 56.2 µmol) was dissolved in absolute ethanol (7 ml) with water (0.25 ml) and glacial acetic acid (2 µl). The solution was hydrogenated over 10% Pd/C (152 mg) at 50 PSI at room temperature for 1 hour. When TLC (ethyl acetate:acetic acid:methanol:water 12:3:3:1; R_f = 0.14 for the compound (48) showed complete conversion, the reaction mixture was filtered through a layer of celite and concentrated. The crude, solid residue (46 mg) was used in the next reaction without further purification.

NMR-data: ^{13}C (D_2O): δ 16.59 (CH_3 fucose), 21,85 ($NHCOCH_3$), 39.44 (CH_2-N), 54.56 (C-2), 60.45-76.95 (C3,4,5,6, C2',3',4',5',6', 2",3",4",5") 99.29, 99.92, 101.28 (C-1, C-1', C-1''), 173.48 ($NHCOCH_3$).

(vii) 2-acrylamidoethyl 2-acetamido-2-deoxy-3-O-2-O-α-L-fucopyranosyl-β-D-galact pyranosyl-β-D-glucopyranoside (49)

The crude compound (48) (46 mg) was dissolved in aqueous ammonia (25%, 4 ml) and stirred at room temperatur. The reaction was complete within 1 hour and yielded the free amin derivative exclusively. (TLC ethyl acetate:acetic acid:methanol :water 5:3:3:1). Concentration and co-concentration with toluene was followed by purification on a Bond-Elut® (SCX, H^+-form) cation exchange resin 0.5 g cartridge. The sample was dissolved in 3 ml of water and pH was adjusted to pH 6 with aqueous acetic acid. The sample was put on the column and then eluted with 2M ammonia in methanol:water, 1:1 (5 ml). The fractions containing free amine (ninhydrin positive) were pooled, concentrated and lyophilized to give (30 mg, 0.05 mmol) crude amine.

1 ml deaerated 0.5 M sodiumborate (aq buffer (pH 8.5) and deaerated methanol (3 ml) was added to the crude amine. The reaction mixture was flushed with nitrogen and cooled to 0°C, 6.4 µl (0.078 mmol) acryloylchloride was added and stirring was continued for 10 minutes. The reaction mixture was concentrat d at room temperature to about a third of its original volume. Purification on a Bio-Gel® P2 column and lyophilization gave 49 of the title compound (49) (30 mg, 86% from (47)).

NMR-data: ^{13}C (D_2O): δ 14.99 (-CH_3, fucose), 21.99 (NHCOCH_3), 39.10 (CH_2N), 54.58 (C-2) 99.25, 99.93, 101.39 (C-1, C'-1, C"-1), 127.27, 129.65 (CH=CH_2).

(viii) Fucα1-2Galβ1-3GlcNAcβ1-O-spacer 5-PAA (50)

Copolymerization of 2-acrylamidoethyl 2-acetamido-2-deoxy-3-O-2-O-α-L-fucopyranosyl-β-D-galactopyranosyl-β-D-glucopyranoside (49) with acrylamide.

T acrylamide (10 mg, 144 µmol) was added at room temperature a solution f the trisaccharide (49) (18 mg, 29 µmol) in

deaerated water (1 ml). To this slowly stirred solution (kept in the dark and under nitr gen) was added at 0°C, first N,N,N',N'-tetramethylethylenediamine (6 µl), and then ammonium persulphate (3.5 mg). The mixture was stirred at room temperature over night. TLC (ethyl acetate:acetic acid:methanol :water 5:3:3:2) showed that almost all of the compound (49) was consumed and that a charring baseline product had been formed. The polymer was purified by gel chromatography on a Bio-Gel® P-2 column eluted with aqueous n-butanol (1%). Freeze-drying of the polymeric fraction eluted in the void volume gave 13.1 mg of the polymer (50) were the ^{1}H NMR analysis of the product showed an average incorporation of 1 trisaccharide per 7.6 acrylamide units, and 11.9 mg of polymer (50) were the ^{1}H NMR analysis of the product showed an average incorporation of 1 trisaccharide per 10.3 acrylamide units.

EXAMPLE 12

Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-O-spacer 5-PAA (55)

(i) 2-azidoethyl 2-acetamido-6-O-benzyl-3-O-(3,4,6-tri-O-benzyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (51).

Diethyl ether saturated with hydrogen chloride was added, at roomtemperature, to a stirred mixture of 2-azidoethyl 2-acetamido-3-O-3,4,6-tri-O-benzyl-β-D-galactopyranosyl-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (45) (420 mg, 0.52 mmol), sodium cyanoborohydrids (200 mg, 3,2 mmol) and molecular sieves 3Å in tetrahydrofuran (20 ml) until the mixture was acidic (as determined with indicator paper; method according to M. Nilsson and T. Norberg Carbohydr. Res., 183 (1988 71-82). The mixture was stirred for 20 min. at roomtemperature and then triethylamine (0.30 mL) was added. The mixture was filtered through Celite, washed with water, dried and evaporated. The crude product was purified by column chromatography (toluene: ethyl acetate, 6:1) t give pure c mp und (51) (266 mg, 0.32 mmol, 65%).

NMR-data: ^{13}C ($CDCl_3$): δ 23.41 ($NHCOCH_3$), 50, 30 (CH_2N), 56, 81 (C-N), 66,3-81,9 (C-3,4,5,6; C-2',3',4',5',6'; 4xCH_2Ph; CH_2O) 100.90, 103.21 (C-1, C-1'), 173,4 (CO)

(ii) 2-azidoethyl 2-acetamido-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-3-O-[3,4,6-tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (52).

The compound (51) (157 mg, 0.19 mmol) and the compound (14) (362 mg, 0.76 mmol) were dissolved in dichloromethane (100 ml), and 3g 4Å molecular sieve (MS) were added and stirred for 20 min. Dimethyl (methylthio)sulfonium triflate (DMTST) (207 mg, 0.80 mmol) was added and stirring was continued for 1.5 hour. 2 ml of triethylamine was added and stirring was continued for another 20 min. Filtration through celite, concentration and column chromatography (toluen:ethylacetate, 1:1) gave the title compound (52) (142 mg, 0.086 mmol, 45%).

NMR-data: ^{13}C ($CDCl_3$): δ 17.01, 16.81 (2xCH_3 fucose), 23.20 ($NHCOCH_3$), 50.35 (CH_2-N), 57.21 (C-2), 98.31, 99.70, 101.14, 102.30 (C1, C1', 2xC1-fucose), 170.30 (C=O).

(iii) 2-trifluoroacetamidoethyl 2-acetamido-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-3-O-[3,4,6 tri-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-β-D-glycopyranoside (53).

The compound (52) (140 mg, 0.084 mmol) was dissolved in 11 ml ethanol and 10% Pd/C (150 mg) was added. The reaction mixtur was hydrogenated at atmospheric pressure for 15 minutes. Analysis by TLC (ethyl acetate:methanol:acetic acid:water 12:3:3:1) showed no starting material, but one ninhydrin positive product. The mixtures was filtered through celite, concentrated and dissolved in dichlor methane (10 ml) and pyridin (3.5 ml), flush d with nitr gen and cooled to 0°C.

Trifluoroacetic anhydride (31 µl, 0.22 mmol) was added. After one hour the mixture was concentrated and coevaporated with 2 ml of toluene twice. Column chromatography (toluene:ethyl acetate 1:2) gave the compound (53) (82.8 mg, 0.053 mmol, 63%).

NMR-data: ^{13}C ($CDCl_3$): δ 17.33, 16.93 (2xCH_3 fucose), 22.30 ($NHCOCH_3$), 39.25 (CH_2-N), 54.48 (C-2), 99.03, 99.98, 101.63, 102.75, (C1, C1', 2xC1-fucose), 171.73 ($NHCOCH_3$).

(iv) 2-trifluoroacetamidoethyl 2-acetamido-2-deoxy-3-O-(2-O-α-L-fucopyranosyl-β-D-galactopyranosyl)-4-O-α-L-fucopyranosyl-β-D-glucopyranoside (54).

The tetrasaccharide (53) (78 mg, 0.05 mmol) was dissolved in absolute ethanol (8 ml) with water (0.25 ml) and glacial acetic acid (2 µL). The solution was rapidly stirred with 10% Pd/C (150 mg) under hydrogen (50 PSI) at room temperature for 1 hour. When TLC (ethyl acetate:acetic acid:methanol:water 12:3 3:1; showed complete conversion, the reaction mixture was filtered thorugh a layer of celite and concentrated. The crude compound (54) (35 mg) was used in the next reaction without further purification.

NMR-data: ^{13}C ($CDCl_3$): δ 16.91, 16.53 (2xCH_3 fucose), 22.15 ($NHCOCH_3$), 39.14 (CH_2N), 54.20 (C-2), 99.33, 100.03, 101.73, 102.95 (C-1, C-1', 2xC-1 fucose), 173.30 ($NHCOCH_3$) there were no ^{13}C signals in the "aromatic region".

(v) 2-acrylamidoethyl 2-acetamido-2-deoxy-3-O-(2-O-(α-L-fucopyranosyl-β-D-galactopyranosyl)-4-O-α-L-fucopyranosyl-β-D-glucopyranoside (55).

35 mg of the crude compound (54) was dissolved in aqueous ammonia (25%, 4 ml) and stirred at room temperature. The reacti n was complete within 1 hour and yielded the free amino derivative exclusively. TLC (ethylacetat :acetic acid: methanol:water, 5:3:3:2), concentration and c -concentration

with toluene was followed by purification on a Bond-Elut® cartridge (SCX, H^+-form) cation exchange resin. The sample was dissolved in 3 ml of water and pH was adjusted to 6 with aqueous acetic acid. The sample was put on the column and then eluted with 2M ammonia in methanol:water, 1:1 (5 ml). The fractions containing free amine (ninhydrin positive) were pooled, concentrated and lyophilized to give crude amine (20 mg). 1 ml Deaerated 0.5 M sodiumborate (aq) buffer (pH 8.5) and deaerated methanol (3 ml) was added to the crude amine. The reaction mixture was flushed with nitrogen and cooled to 0°C. 6 µL acryloylchloride was added and stirring was continued for 10 min. The reaction mixture was concentrated at room temperature to about a third of its original volume. Purification on a Bio-Gel® P2 column and lyophilization gave pure title compound (55) (15 mg).

NMR-data: ^{13}C (D_2O): δ 16.90, 16.45 (2xCH_3 fucose), 21.95 ($NHCOCH_3$) 39.51 (CH_2N), 54.31 (C-2) 99.21, 99.95, 101.56, 102.87 (C-1, C-1', 2xC-1 fucose), 127.21, 129.57 ($CH=CH_2$) 173.27 ($NHCOCH_3$).

(vi) Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-O-spacer 5-PAA (56)

Copolymerization of 2-acrylamidoethyl 2-acetamido-2-deoxy-3-O-2-O-α-L-fucopyranosyl-β-D-galactopyranosyl-4-α-L-fucopyranosyl-β-D-glucopyranoside (55) and acrylamide.

To acrylamide (8.3 mg, 120 µmol) was added at room temperature a solution of tetrasaccharide (54) (15 mg, 20 µmol) in deaerated water (1 ml). To this slowly stirred solution (kept in the dark and under nitrogen atmosphere was added at 0°C, first N,N,N',N'-tetramethylethylenediamine (6 µl), and then ammonium persulphate (3.5 mg). The mixture was stirred at room temperature over night. TLC (ethyl acetate:acetic acid:methanol :water 5:3:2) showed that all of compound (49) was consumed and that a charring baseline product had been formed. The polymer was purified by gel chromatography on a Bio-Gel P-2 column

eluted with aqueous n-butanol (1%). Freeze-drying of the polymeric fraction luted in the void volume gave 20 mg of p lymer (56).

A ^{1}H-NMR analysis of the product showed an average incorporation of 1 trisaccharide per 6 acrylamide units.

EXAMPLE 13

Fucα1-2 Galβ1-O-spacer 5-PAA (58)

(i) 2-acrylamidoethyl 2-O-α-L-fucopyranosyl-β-D-galactopyranoside (57)

0.3 ml deaerated 0.5 M sodiumborate (aq) buffer (pH 8.5) and methanol (0.9 ml) was added to 6.4 mg of the compound (30). The reaction mixture was flushed with nitrogen and cooled to 0°C. 2 µl acryloyl chloride was added and stirring was continued for 10 minutes. The reaction mixture was concentrated at room temperature to about a third of its original volume. Purification on a Bio-Gel® P2 column and lyophilization gave the compound (57) (4 mg, 57%).

NMR-data: ^{1}H (D_2O): δ 1.2 (d, CH_3 fucose) 4.52 (dd, H-1), 5.22 (m, H-1'), 5.80 (dd, $CH=CH_2$), 6.25 (m, $CH=CH_2$).

(ii) Fucα1-2 Galβ1-O-spacer 5-PAA (58)

To a solution of the compound (57) (4 mg, 9 µmol) and acrylamide (3.3 mg, 47 µmol) in deaerated water (0.75 ml) was added first N,N,N',N'-tetramethylenediamine (2 µl) and then ammonium persulphate (1.5 mg). The mixture was stirred at room temperature over night. The polymer (58) was purified on a Bi - Gel® P2 column (9.1 mg).

NMR-data: ^{1}H (D_2O) showed an average incorporation of 1 ligosaccharide per 12.3 acrylamide units.

BIOLOGICAL EXPERIMENTS

Materials and Methods

In situ adherence assay for Helicobacter pylori

Non-infected samples from normal adult human gastric tissue (obtained from Huddinge Sjukhus, Sweden) were used to study *Helicobacter pylori* adherence. All samples were fixed in 4% formalin and subsequently embedded in paraffin.

Sections, 4 μm thick, were placed on glass slides and used f r Steiner's silver staining (to identify the cell types present in gastric units, and to verify that the tissue samples have no pathologic changes) and/or subsequent adherence assay.

Four clinical isolates, A4, A5, A7, and A8 (obtained from Huddinge Sjukhus) of *Helicobacter pylori* were used. *Helicobacter pylori* was cultured at 37°C on Brucella Agar supplemented with 10% bovine blood and 1% IsoVitalex (Becton Dickinson Microbiology System, Cockeyville, MD) under microaerophilic conditions (5% O_2, 10% CO_2, 85% N_2) and 98% humidity. Five days after inoculation, bacteria from one full-grown plate were resuspended by gentle pipetting in 25 ml of 0.1M NaCl/ 0.1M sodium carbonate, pH 9.0. 250 μl of a freshly prepared 10 mg/ml solution of fluorescein isothiocyanate (FITC, Sigma Chemical Co.) in dimethylsulfoxide was added to the suspension of bacteria which was then incubated for 1 hour at room temperature in the dark. The bacteria were recovered by centrifugation at 3000 x g for 10 minutes, and then resuspended in phosphate buffered saline (PBS) + 0.05% polyoxyethylene sorbitan monolaurate (Tween 20) by gentle pipetting and subsequently pelleted by centrifugation as above. The wash procedure was repeated 3 times and the suspension was finally resuspended to an Optical Density of 0.2. The intensity of FITC-labelling of all bacterial strains was similar as judged by inspection of comparable numbers of organisms by fluorescence microsc py. Aliquots of 1 ml were

taken from the final suspensions and utilized immediately or stored at -20°C until use. N difference in binding pattern was observed between strains labelled and used immediately and strains that were frozen and thawed once before use.

Slide-mounted tissue sections were deparaffinized in Bio-Clear (Bio-Optica SpA) and absolute alcohol, 95% alcohol followed by 70% alcohol, rinsed in water followed by PBS and then incubated for 45 minutes in blocking buffer (1% gelatin/0.05% Tween 20 in PBS). FITC labelled bacterial suspension (OD about 0.200-0.250) was mixed with equal amount of a concentrated solution of the compound. The mixture was preincubated for 2 hours at room temperature in the dark, 200 µl of the mixture was placed on a slide-mounted tissue section and incubated for 1 hour at room temperature in a humidified chamber. The slides were subsequently washed 6 times with PBS prior to inspection under fluorescence microscope.

Analysis

The *in situ* adherence assay was used to ascertain binding of *Helicobacter pylori* to human gastric tissue and to demonstrate inhibition of *Helicobacter pylori* with terminal L-fucose-containing compounds, e.g. LNF1-HSA.

To analyze the ability of terminal L-fucose-containing compounds to inhibit binding. FITC labelled bacterial suspension (O.D. about 0.200-0.250) was mixed with equal amount of a concentrated solution of the compound. The mixture was preincubated for 2 hours at room temperature in the dark. 200µl of the mixture was placed on a slide-mounted tissue section and was incubated for 1 hour at room temperature. After incubation, the treated tissue sections were washed 6 times with PBS before analysis of the tissue sections.

Comparison tissue sections treated with test compound with untreated tissue sections using fluorescence micr sc py and image analysis (Neotech Image Grabber 24/1.1 t transfer the

visual microscope image to a computer screen and Optilab 24/2.1.1 Grafted, to count the adhered bacteria).

The given values in the table are the average number of adhered bacteria on three different areas per section comparing treated (with compound) with untreated tissue sections.

Table

COMPOUND	CONC	INHIB (average value)
[Fucα1-2Galβ1-spacer 1]$_5$-HSA	2 mM	34%
[Fucα1-2Galβ1-spacer 4]$_8$-HSA	2 mM	35%
[Fucα1-2Galβ1-spacer 2]$_n$-PAA n=1 per 12.3 acrylamide moieties	2 mM	45%
[Fucα1-2Galβ1-spacer 5]$_n$-PAA n=1 per 5 acrylamide moieties	1 mM	53%
[Fucα1-2Galβ1-3GlcNAcβ1-spacer 2]$_n$-PAA n=1 per 7.6 acrylamide moieties	2 mM	40%
[Fucα1-2Galβ1-3GlcNAcβ1-Galβ1-spacer 3]$_{35}$--HSA (LNF1-HSA) (Purchased from Iso Sep AB, Sweden)	0.2 mM	72%
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-Galβ1--spacer 3]$_{32}$-HSA (LND1-HSA) (Purchased from Iso Sep AB, Sweden)	0.2 mM	71%
[Fucα1-2Galβ1-3Fucα1-4)GlcNacβ1-Galβ1--spacer 3]$_n$-PAA n=1 per 18 acrylamide moieties	0.2 mM	67%
n=1 per 5 acrylamide moieties	0.2 mM	84%
n=1 per 6 acrylamide moieties	0.2 mM	93%
[GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)-GlcNacβ1-Galβ1-spacer 3]$_{22}$-HSA (A-hepta-HSA) (Purchased from Iso Sep AB, Sweden)	0.2 mM	80%

CLAIMS

1. Use of a compound of the general formula Ia, Ib, Ic, Id, Ie or If

$Y\text{-}Z_1\text{-}R$ $A\text{-}Z_2\text{-}R$ $A\text{-}Z_3\text{-}B\text{-}Z_4\text{-}R$

Ia Ib Ic

$A\text{-}Z_5\text{-}B\text{-}Z_6\text{-}C\text{-}Z_7\text{-}R$ $A\text{-}Z_8\text{-}B\text{-}Z_9\text{-}C\text{-}Z_{10}\text{-}D\text{-}Z_{11}\text{-}R$

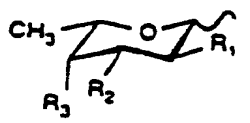
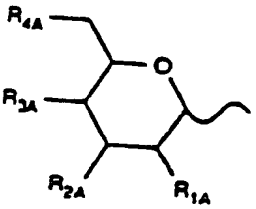
Id Ie

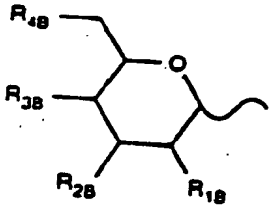
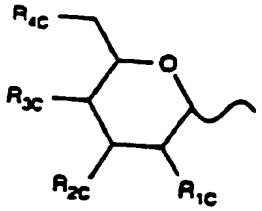
$A\text{-}Z_{12}\text{-}B\text{-}Z_{13}\text{-}C\text{-}Z_{14}\text{-}D\text{-}Z_{15}\text{-}E\text{-}Z_{16}\text{-}R$

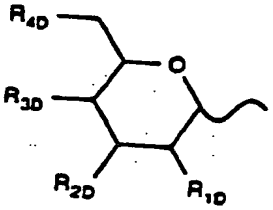
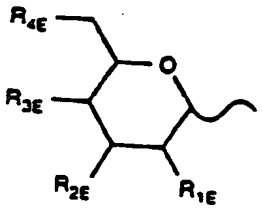
If

wherein

Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} independently are O, S, CH_2, or NR_{25}, where R_{25} is hydrogen, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl optionally substituted with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

Y is  ; A is  ;

B is  ; C is  ;

D is  ; E is  ;

wherein

the wavy line in Y, A, B, C, D and E signifies a bond which is either in the α- or in the β-configuration;

R_1, R_2, and R_3 each independently are H, halogen, azid , guanidinyl, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl or aryl-C_{1-4}-alkyl optionally substituted in the aryl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4}-alkyl)silylethyl; oxo;

a group $=CR_4R_5$ wherein R_4 and R_5 independently are H, or C_{1-4}-alkyl;

or a group XR_{10} wherein X is O, S, NR_{20}, or =N-, and R_{10} is H, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl, aryl-C_{1-4}-alkyl, or heterocyclyl-C_{1-4}-alkyl optionally substituted in the aryl or heterocyclyl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4} alkyl)silylethyl; tri(C_{1-4}-alkyl)silyl; tri(C_{1-4}-alkyl)silylethoxymethyl; the acyl residue of a naturally occurring amino acid; C_{1-24}-alkylcarbonyl; C_{2-24}-alkenylcarbonyl; C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl; arylcarbonyl; or terpenyl; and

R_{20} is H, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl or phthaloyl optionally substituted in the benzene ring with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alk xy, nitr , halogen, phen xy, or mono- r di-halogen-C_{1-4}-alkyl;

R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} each independently is as defined for R_1, R_2, and R_3 above, or is a group of the formula VII

$$YZ_1 \qquad \text{VII}$$

wherein Y and Z_1 are as defined above;
with the provisos
that one of R_{1B}, R_{2B}, R_{3B}, or R_{4B} is Z_3, Z_5, Z_8 or Z_{12}, that one of R_{1C}, R_{2C}, R_{3C}, or R_{4C} is Z_6, Z_9 or Z_{13}, that one of R_{1D}, R_{2D}, R_{3D}, or R_{4D} is Z_{10}, or Z_{14},
that one of R_{1E}, R_{2E}, R_{3E}, or R_{4E} is Z_{15},
that at least one and at the most five of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} is a group of the formula VII, and
that the configurations of the substituents R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A, the configurations of the substituents R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B, the configurations of the substituents R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C, the configurations of the substituents R_{1D}, R_{2D}, R_{3D}, and $R_{4D}CH_2$ in D, and the configurations of the substituents R_{1E}, R_{2E}, R_{3E}, and $R_{4E}CH_2$ in E independently are D-gluco, L-gluco, D-galacto, L-galacto, D-manno, L-manno, D-talo, L-talo, D-allo, L-allo, D-altro, L-altro, D-gulo, L-gulo, D-ido, or L-ido;

R is hydrogen, a branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, C_{1-12}-alkoxy-C_{1-12}-alkyl, C_{1-24}-alkylcarbonyl, C_{2-24}-alkenylcarbonyl, or C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; an aryl, aryl-C_{1-4}-alkyl, arylcarbonyl or aryl-C_{1-4}-alkylcarb nyl group optionally substituted in the aryl moi ty with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- r

di-halogen-C_{1-4}-alkyl; terpenyl;
tri(C_{1-4}-alkyl)silylethyl; heterocyclyl;
h terocyclyl-C_{1-4}-alkyl; or
heterocyclyl-C_{1-4}-alkylcarbonyl;

a group of the formula II or IIa

$$R_{30}-(CH_2)_q-S(O)_m-CH_2CH_2- \qquad II$$
$$[R_{30}-(CH_2)_q-S(O)_m-CH_2]_2CH-CH_2- \qquad IIa$$

wherein R_{30} is H, carboxy, C_{1-4}-alkoxycarbonyl, hydroxy, amino, or a matrix MA, q is an integer fr m 1 to 24, and m is 0 or 2; or

a group of the formula III or IIIa

$$Phe-S(O)_m-CH_2CH_2- \qquad III$$
$$[Phe-S(O)_m-CH_2]_2CH-CH_2- \qquad IIIa$$

wherein m is as defined above, and each Phe is phenyl optionally substituted with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy or mono- or di-halogen C_{1-4}-alkyl; or phenyl-C_{1-4}-alkyl optionally monosubstituted in the phenyl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

a group of the formula IV

$$R_{40}CH_2CH(CH_2R_{50})CH_2- \qquad IV$$

wherein R_{40} and R_{50} independently are halogen; or

a group Q-(Spacer)$_r$-, where r is an integer 0 or 1 and Q is a matrix MA or a group -COO-MA;

for the preparation of a pharmaceutical composition for the treatment or prophylaxis in humans of conditions involving infection by *Helicobacter pylori* of human gastric mucosa.

2. Use according to claim 1 in which Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} are O.

3. Use according to claim 1 or 2 in which at the most four, preferably at the most three, in particular one or two of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E} or R_{4E} is a group of formula VII.

4. Use according to any of claims 1-3 in which R_{1A} is a group VII in the α-configuration.

5. Use according to any of claims 1-3 in which the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration.

6. Use according to any of claims 1-3 in which R_{1A} is a group VII in the α-configuration and the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration.

7. Use according to any of claims 1-3 in which R_{2B} is Z_3, Z_5, Z_8, or Z_{12}, and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration.

8. Use according to any of claims 1-3 in which R_{1B} is an acetamido group.

9. Use according to any of claims 1-3 in which R_{1A} is a group VII in the α-configuration; the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration; R_{2B} is Z_3, Z_5, Z_8, or Z_{12}; and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration and R_{1B} is an acetamido group.

10. Use according to any of claims 1-9 in which R_{3B} is a group of the formula VII in the α-configuration.

11. Use according to any of claims 1-10 in which the configurations of R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A and of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-galacto, and the configurations of R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C are D-gluco, A being in the α-configuration, and B and C being in the β-configuration, and in which R_{1B} and R_{3C} are groups of the formula VII in the α-configuration, and in which R_{1A} and R_{1C} are acetamido groups, and R_{2B} is Z_5, Z_8 or Z_{12}, and R_{2C} is Z_6, Z_9 or Z_{13}.

12. Use according to claim 6 in which A is Fucα1-2Galβ.

13. Use according to claim 9 in which A-Z_3-B is
Fucα1-2Galβ1-3GlcNAcβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ.

14. Use according to claim 9 in which A-Z_5-B-Z_6-C is
Fucα1-2Galβ1-3GlcNAcβ1-3Galβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ.

15. Use according to claims 9 or 11 in which A-Z_8-B-Z_9-C-Z_{10}-D is

GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ.

16. Use according to claim 11 in which A-Z_{12}-B-Z_{13}-C-Z_{14}-D-Z_{15}-E is
GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ.

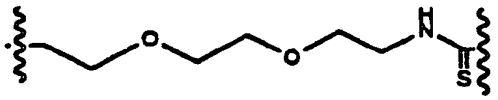
17. Use according to any of claims 1-16 in which R is a group Q-(Spacer)$_r$-, where r is an integer 0 or 1 and Q is a matrix MA.

18. Us according to any f claims 1-17 in which the Spacer is defined $(W)_v$-S'-P', wher in S' is an C_{1-24} alkyl, an C_{2-24} alkenyl, an C_{1-24}alkylaryl, an arylC_{1-24}alkyl an arylC_{1-24}alkylaryl, an C_{1-24}alkylarylC_{1-24}alkyl group which groups may be interrupted by carbonyl, thiocarbonyl, oxycarbonyl, carbonyloxy, carbonylamino, aminocarbonyl, aza, oxa or thia groups; an aryl group, an aryloxy, an C_{1-24}alkoxy, a polyethyleneglycol group, a steroid group, a sphingoid group; all groups may be substituted with carboxyl, C_{1-4}alkylcarbonyl, amide, hydroxy, alkoxy, aryloxy, phenoxy;

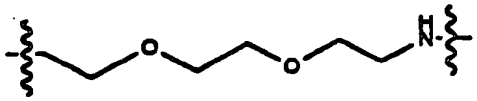
P' is NH-C(S), NH-C(O), C(O), NH, C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_3, PO_4;
W is NH-C(S), NH-C(O), C(O), C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_2, PO_3, PO_4,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are CH_2 then W cannot be PO_2,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are O or S then W cannot be (O)CO, SO_4 or PO_4, and with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are NH then W cannot be NH-C(S), NH-C(O), (O)CO, SO_4, PO_4; and v is an integer 0 or 1.

19. Use according to any of claim 18 in which the spacer is selected from

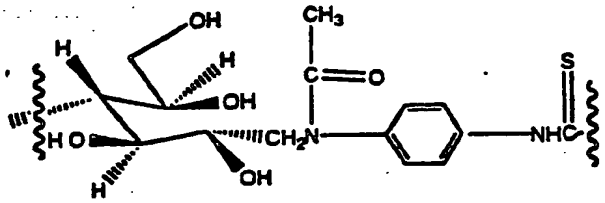
spacer 1



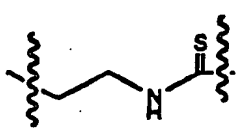
spacer 2



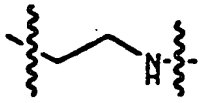
spacer 3



spacer 4



spacer 5



20. Use according to claims 1-17 in which MA is HSA, BSA or PAA.

21. Use according to claim 1 in which the compound is selected from

$[Fuc\alpha1\text{-}2Gal\beta1\text{-}Spacer]_n\text{-}MA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3GlcNAc\beta\text{-}Spacer]_n\text{-}MA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta\text{-}Spacer]_n\text{-}MA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer]_n\text{-}MA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer]_n\text{-}MA$;
$[GalNAc\alpha1\text{-}3(Fuc\alpha1\text{-}2)Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer]_n\text{-}MA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}4Glc\beta1\text{-}NH]_nMA$;
$[GalNAc\alpha1\text{-}3(Fuc\alpha1\text{-}2)Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}4Glc\beta1\text{-}Spacer]_n\text{-}MA$;

wherein the Spacer is selected from the group defined in claim 19, n is an integer 1-40 when MA is HSA or BSA, and n is an interger 10-10000 when MA is PAA.

22. Use according to claim 1 in which the compound is selected from

$[Fuc\alpha1\text{-}2Gal\beta1\text{-}Spacer\ 1]_n\text{-}HSA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}Spacer\ 2]_n\text{-}PAA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}Spacer\ 4]_n\text{-}HSA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}Spacer\ 5]_n\text{-}PAA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3GlcNAc\beta\text{-}Spacer\ 5]_n\text{-}PAA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta\text{-}Spacer\ 5]_n\text{-}PAA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer\ 3]_n\text{-}HSA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer\ 3]_n\text{-}HSA$;
$[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}4Glc\beta1\text{-}NH]_n\text{-}PAA$;
$[GalNAc\alpha1\text{-}3(Fuc\alpha1\text{-}2)Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc\beta1\text{-}3Gal\beta1\text{-}Spacer\ 3]_n$-
-HSA;

wherein Spacer 1, Spacer 2, Spacer 3, Spacer 4 and Spacer 5 are defined as in claim 19 and n is an integer 1-40 when MA is HSA, and n is an interger 10-10000 when MA is PAA.

23. Use according to any of claims 1-22 wherein the compound f formula Ia, Ib, Ic, Id, Ie r If is adapted to be administered in combination with a preparation for standard therapy of gastritis r ulcus, especially preparations containing

omeprazole, cimetidine, ranitidine, lansoprazole, pantoprazole, sucralfate, famotidine, niz tidine, magnesium hydroxide, aluminium hydroxide, calcium carbonate, simethicone or magaldrate.

24. Use according to any of claims 1-23 wherein the compound of formula Ia, Ib, Ic, Id, Ie or If is adapted to be administered in combination with a preparation for a course of therapy with an antimicrobial agent, especially preparations containing:

β-lactam antibiotics such as amoxicillin, ampicillin, cephalothin, cefaclor or cefixime; or
macrolides such as erythromycin, or clarithromycin; or
tetracyclines such as tetracycline or doxycycline; or
aminoglycosides such as gentamycin, kanamycin or amikacin; or
quinolones such as norfloxacin, ciprofloxacin or enoxacin; r
others such as metronidazole, nitrofurantoin or chloramphenicol;
or preparations containing bismuth salts such as bismuth subcitrate, bismuth subsalicylate, bismuth subcarbonate, bismuth subnitrate or bismuth subgallate.

25. A method of treating and/or preventing diseases in humans caused by infection by *Helicobacter pylori* of human gastric mucosa, said method comprising administering to a patient in need thereof an effective amount of a compound of the formula Ia, Ib, Ic, Id, Ie or If as defined in claims 1-22.

26. A method of treating and/or preventing diseases in humans caused by infection by *Helicobacter pylori* of human gastric mucosa, said method comprising administering to a patient in need thereof an effective amount of a compound of the formula Ia, Ib, Ic, Id, Ie of If as defined in claims 1-22 in combination with at least one anti-ulcer or anti-gastritis medicament, or with at least one antimicrobial agent, or with mixtures th re f.

27. A pharmaceutical composition comprising a compound of the formula Ia, Ib, Ic Id, Ie or If as defined in claims 1-22 or a mixture of such compounds, in combination with at 1 ast one anti-ulcer or anti-gastritis medicament, or with at least one antimicrobial agent, or with mixtures thereof, and with a pharmaceutically acceptable carrier.

28. A pharmaceutical composition according to claim 27 in which the anti-ulcer or anti-gastritis medicament is selected from a gastric secretion inhibiting compound and an antacid.

29. A pharmaceutical composition according to claim 28 in which the gastric secretion inhibiting compound is selected from cimetidine, ranitidine, famotidine, nizatidine, omeprazole, lansoprazole, pantoprazole, and sucralfate.

30. A pharmaceutical composition according to claim 28 in which the antacid is selected from $Al(OH)_3$, $Mg(OH)_2$, $CaCO_3$, Na_2CO_3, $NaHCO_3$, aluminium magnesium hydroxide or its hydrate, simethicone.

31. A pharmaceutical composition according to claim 27 in which the antimicrobial agent is selected from β-lactam antibiotics such as amoxicillin, ampicillin, cephalothin, cefaclor or cefixime; macrolides such as erythromycin or clarithromycin; tetracyclines such as tetracycline or doxycycline; aminoglycosides such as gentamycin, kanamycin or amikacin; quinolones such as norfloxacin, ciprofloxacin or enoxacin; bismuth salts such as bismuth subcitrate, bismuth subsalicylate, bismuth subcarbonate, bismuth subnitrate or bismuth subgallate; heterocyclic antibiotics such as metronidazole or nitrofurantoin; and benzene derivatives such as chloramphenic 1.

32. Novel compounds of the general formula Ia, Ib, Ic, Id, Ie r If

$Y\text{-}Z_1\text{-}R$ $A\text{-}Z_2\text{-}R$ $A\text{-}Z_3\text{-}B\text{-}Z_4\text{-}R$

Ia Ib Ic

$A\text{-}Z_5\text{-}B\text{-}Z_6\text{-}C\text{-}Z_7\text{-}R$ $A\text{-}Z_8\text{-}B\text{-}Z_9\text{-}C\text{-}Z_{10}\text{-}D\text{-}Z_{11}\text{-}R$

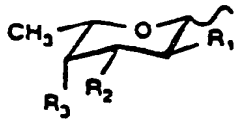
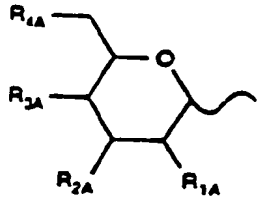
Id Ie

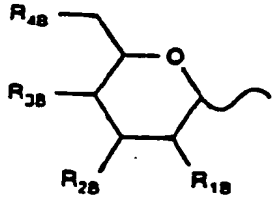
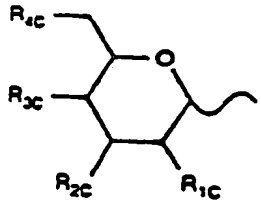
$A\text{-}Z_{12}\text{-}B\text{-}Z_{13}\text{-}C\text{-}Z_{14}\text{-}D\text{-}Z_{15}\text{-}E\text{-}Z_{16}\text{-}R$

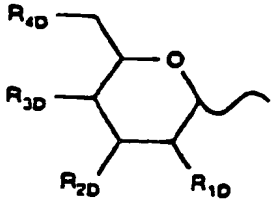
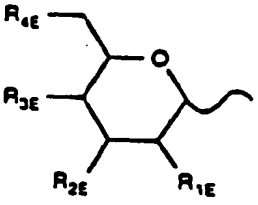
If

wherein

Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} independently are O, S, CH_2, or NR_{25}, where R_{25} is hydrogen, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl optionally substituted with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

Y is  ; A is  ;

B is  ; C is  ;

D is  ; E is 

wherein

the wavy line in Y, A, B, C, D and E signifies a bond which is either in the α- or in the β-configuration;

R_1, R_2, and R_3 each independently are H, halogen, azido, guanidinyl, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl or aryl-C_{1-4}-alkyl optionally substituted in the aryl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4}-alkyl)silylethyl; oxo;

a group $=CR_4R_5$ wherein R_4 and R_5 independently are H, or C_{1-4}-alkyl;

or a group XR_{10} wherein X is O, S, NR_{20}, or =N-, and R_{10} is H, branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, or C_{1-12}-alkoxy-C_{1-12}-alkyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; aryl, aryl-C_{1-4}-alkyl, or heterocyclyl-C_{1-4}-alkyl optionally substituted in the aryl or heterocyclyl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl; tri(C_{1-4} alkyl)silylethyl; tri(C_{1-4}-alkyl)silyl; tri(C_{1-4}-alkyl)silylethoxymethyl; the acyl residue of a naturally occurring amino acid; C_{1-24}-alkylcarbonyl; C_{2-24}-alkenylcarbonyl; C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl; arylcarbonyl; or terpenyl; and

R_{20} is H, C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{1-24}-alkylcarbonyl, or benzoyl or phthaloyl optionally substituted in the benzene ring with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} each independently is as defined f r R_1, R_2, and R_3 above, r is a group of the formula VII

VII

wherein Y and Z_1 are as defined above;
with the provisos
that one of R_{1B}, R_{2B}, R_{3B}, or R_{4B} is Z_3, Z_5, Z_8 or Z_{12},
that one of R_{1C}, R_{2C}, R_{3C}, or R_{4C} is Z_6, Z_9 or Z_{13}, that one of R_{1D}, R_{2D}, R_{3D}, or R_{4D} is Z_{10}, or Z_{14},
that one of R_{1E}, R_{2E}, R_{3E}, or R_{4E} is Z_{15},
that at least one and at the most five of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E}, and R_{4E} is a group of the formula VII, and
that the configurations of the substituents R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A, the configurations of the substituents R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B, the configurations of the substituents R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C, the configurations of the substituents R_{1D}, R_{2D}, R_{3D}, and $R_{4D}CH_2$ in D, and the configurations of the substituents R_{1E}, R_{2E}, R_{3E}, and $R_{4E}CH_2$ in E independently are D-gluco, L-gluco, D-galacto, L-galacto, D-manno, L-manno, D-talo, L-talo, D-allo, L-allo, D-altro, L-altro, D-gulo, L-gulo, D-ido, or L-ido;

R is hydrogen, a branched or unbranched C_{1-24}-alkyl, C_{2-24}-alkenyl, C_{2-24}-alkynyl, C_{3-8}-cycloalkyl, C_{3-8}-cycloalkyl-C_{1-24}-alkyl, C_{1-12}-alkoxy-C_{1-12}-alkyl, C_{1-24}-alkylcarbonyl, C_{2-24}-alkenylcarbonyl, or C_{3-8}-cycloalkyl-C_{1-24}-alkylcarbonyl group which is optionally substituted with hydroxy, amino, halogen, or oxo; an aryl, aryl-C_{1-4}-alkyl, arylcarbonyl or aryl-C_{1-4}-alkylcarbonyl group optionally substituted in the aryl moi ty with hydr xy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phen xy, or mono- or

di-halogen-C_{1-4}-alkyl; terpenyl;
tri(C_{1-4}-alkyl)silylethyl; heterocyclyl;
heterocyclyl-C_{1-4}-alkyl; or
heterocyclyl-C_{1-4}-alkylcarbonyl;

a group of the formula II or IIa

$$R_{30}-(CH_2)_q-S(O)_m-CH_2CH_2- \qquad II$$
$$[R_{30}-(CH_2)_q-S(O)_m-CH_2]_2CH-CH_2- \qquad IIa$$

wherein R_{30} is H, carboxy, C_{1-4}-alkoxycarbonyl, hydroxy, amino, or a matrix MA, q is an integer from 1 to 24, and m is 0 or 2; or

a group of the formula III or IIIa

$$Phe-S(O)_m-CH_2CH_2- \qquad III$$
$$[Phe-S(O)_m-CH_2]_2CH-CH_2- \qquad IIIa$$

wherein m is as defined above, and each Phe is phenyl optionally substituted with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy or mono- or di-halogen C_{1-4}-alkyl; or phenyl-C_{1-4}-alkyl optionally monosubstituted in the phenyl moiety with hydroxy, amino, C_{1-4}-alkyl, C_{1-4}-alkoxy, nitro, halogen, phenoxy, or mono- or di-halogen-C_{1-4}-alkyl;

a group of the formula IV

$$R_{40}CH_2CH(CH_2R_{50})CH_2- \qquad IV$$

wherein R_{40} and R_{50} independently are halogen; or

a group Q-(Spacer)$_r$-, where r is an integer 0 or 1 and Q is a matrix MA or a group -COO-MA.

33. Novel comp unds according to claim 32 in which Z_1, Z_2, Z_3, Z_4, Z_5, Z_6, Z_7, Z_8, Z_9, Z_{10}, Z_{11}, Z_{12}, Z_{13}, Z_{14}, Z_{15} and Z_{16} are O.

34. Novel compounds according t any of claims 1 or 2 in which at the m st f ur, preferably at the most three, in particular one or two of R_{1A}, R_{2A}, R_{3A}, R_{4A}, R_{1B}, R_{2B}, R_{3B}, R_{4B}, R_{1C}, R_{2C}, R_{3C}, R_{4C}, R_{1D}, R_{2D}, R_{3D}, R_{4D}, R_{1E}, R_{2E}, R_{3E} or R_{4E} is a group of formula VII.

35. Novel compounds according to any of claims 32-34 in which R_{1A} is a group VII in the α-configuration.

36. Novel compounds according to any of claims 32-34 in which the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration.

37. Novel compounds according to any of claims 32-34 in which R_{1A} is a group VII in the α-configuration and the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration.

37. Novel compounds according to any of claims 32-34 in which R_{2B} is Z_3, Z_5, Z_8, or Z_{12}, and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration.

39. Novel compounds according to any of claims 32-34 in which R_{1B} is an acetamido group.

40. Novel compounds according to any of claims 32-34 in which R_{1A} is a group VII in the α-configuration; the configuration of R_{1A}, R_{2A}, R_{3A} and $R_{4A}CH_2$ in A are D-galacto, A being in the β-configuration; R_{2B} is Z_3, Z_5, Z_8, or Z_{12}; and the configuration of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-gluco, B being in the β-configuration and R_{1B} is an acetamido group.

41. Novel compounds according to any of claims 32-40 in which R_{3B} is a group of the formula VII in the α-configuration.

42. Novel compounds according to any of claims 32-41 in which the configurations of R_{1A}, R_{2A}, R_{3A}, and $R_{4A}CH_2$ in A and of R_{1B}, R_{2B}, R_{3B}, and $R_{4B}CH_2$ in B are D-galacto, and the configurations of

R_{1C}, R_{2C}, R_{3C}, and $R_{4C}CH_2$ in C are D-gluco, A being in the α-configuration, and B and C being in the β-configurati n, and in which R_{1B} and R_{3C} are groups of the formula VII in the α-configuration, and in which R_{1A} and R_{1C} are acetamido groups, and R_{2B} is Z_5, Z_8 or Z_{12}, and R_{2C} is Z_6, Z_9 or Z_{13}.

43. Novel compounds according to claim 37 in which A is Fucα1-2Galβ.

44. Novel compounds according to claim 40 in which A-Z_3-B is Fucα1-2Galβ1-3GlcNAcβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ.

45. Novel compounds according to claim 40 in which A-Z_5-B-Z_6-C is

Fucα1-2Galβ1-3GlcNAcβ1-3Galβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ.

46. Novel compounds according to claims 40 or 42 in which A-Z_8-B-Z_9-C-Z_{10}-D is
GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ; or
Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ.

47. Novel compounds according to claim 42 in which A-Z_{12}-B-Z_{13}-C-Z_{14}-D-Z_{15}-E is
GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ.

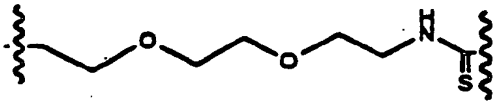
48. Novel compounds according to any of claims 32-47 in which R is a group Q-(Spacer)$_r$-, where r is an integer 0 or 1 and Q is a matrix MA.

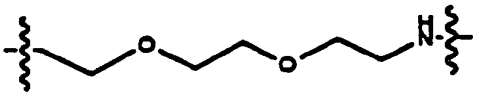
49. Novel compounds according to any of claims 32-48 in which the Spacer is defined (W)$_v$-S'-P', wherein S' is an C_{1-24} alkyl, an C_{2-24} alkenyl, an C_{1-24}alkylaryl, an arylC_{1-24}alkyl an arylC_{1-24}alkylaryl, an C_{1-24}alkylarylC_{1-24}alkyl group which groups may be interrupted by carbonyl, thiocarbonyl, oxycarb nyl, carbonyloxy, carbonylamino, aminocarb nyl, aza, oxa or thia groups; an aryl group, an aryloxy, an C_{1-24}alkoxy, a p lyethyleneglycol group, a

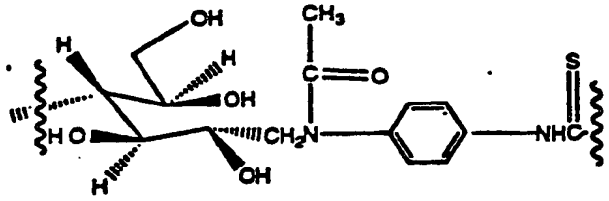
steroid group, a sphingoid group; all groups may b substituted with carboxyl, C_{1-4}alkylcarbonyl, amide, hydroxy, alk xy, aryloxy, phenoxy;

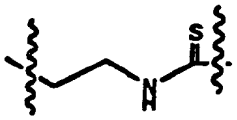
P' is NH-C(S), NH-C(O), C(O), NH, C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_3, PO_4;
W is NH-C(S), NH-C(O), C(O), C(S), C(O)O, (O)CO, SO, SO_2, SO_3, SO_4, PO_2, PO_3, PO_4,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are CH_2 then W cannot be PO_2,
with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are O or S then W cannot be (O)CO, SO_4 or PO_4, and with the proviso that when Z_1, Z_2, Z_4, Z_7, Z_{11} or Z_{16} are NH then W cannot be NH-C(S), NH-C(O), (O)CO, SO_4, PO_4; and v is an integer 0 or 1.

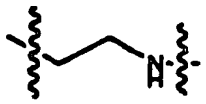
50. Novel compounds according to any of claims 49 in which the spacer is selected from

spacer 1 

spacer 2 

spacer 3 

spacer 4 

spacer 5 

51. Novel compounds according to claims 32-51 in which MA is HSA, BSA or PAA.

52. Novel comp unds according to claim 32 in which the compound is selected from
[Fucα1-2Galβ1-Spacer]$_n$-MA;
[Fucα1-2Galβ1-3GlcNAcβ-Spacer]$_n$-MA;
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ-Spacer]$_n$-MA;
[Fucα1-2Galβ1-3GlcNAcβ1-3Galβ1-Spacer]$_n$-MA;
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer]$_n$-MA;
[GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-Spacer]$_n$-MA;
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-NH]$_n$MA;
[GalNAcα1-3(Fucα1-2)Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-Spacer]$_n$-MA;

wherein the Spacer is selected from the group defined in claim 50, n is an integer 1-40 when MA is HSA or BSA, and n is an interger 10-10000 when MA is PAA.

53. Novel compounds according to claim 32 in which the compound is selected from
[Fucα1-2Galβ1-Spacer 1]$_n$-HSA;
[Fucα1-2Galβ1-Spacer 2]$_n$-PAA;
[Fucα1-2Galβ1-Spacer 4]$_n$-HSA;
[Fucα1-2Galβ1-Spacer 5]$_n$-PAA;
[Fucα1-2Galβ1-3GlcNAcβ-Spacer 5]$_n$-PAA;
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ-Spacer 5]$_n$-PAA;
[Fucα1-2Galβ1-3(Fucα1-4)GlcNAcβ1-3Galβ1-4Glcβ1-NH]$_n$-PAA;

wherein Spacer 1, Spacer 2, Spacer 3, Spacer 4 and Spacer 5 are defined as in claim 50 and n is an integer 1-40 when MA is HSA, and n is an interger 10-10000 when MA is PAA.

54. Novel compounds according to any of claims 32-53 wherein the compound of formula Ia, Ib, Ic, Id, Ie or If is adapted to be administered in combination with a preparation for standard therapy of gastritis or ulcus, especially preparations containing omeprazole, cimetidine, ranitidine, lansoprazole, pantoprazole, sucralfate, famotidin , nizetidine, magnesium

hydroxide, aluminium hydroxide, calcium carbonate, simethicone or magaldrate.

55. Novel compounds according to any of claims 32-54 wherein the compound of formula Ia, Ib, Ic, Id, Ie or If is adapted to b administered in combination with a preparation for a course of therapy with an antimicrobial agent, especially preparations containing:

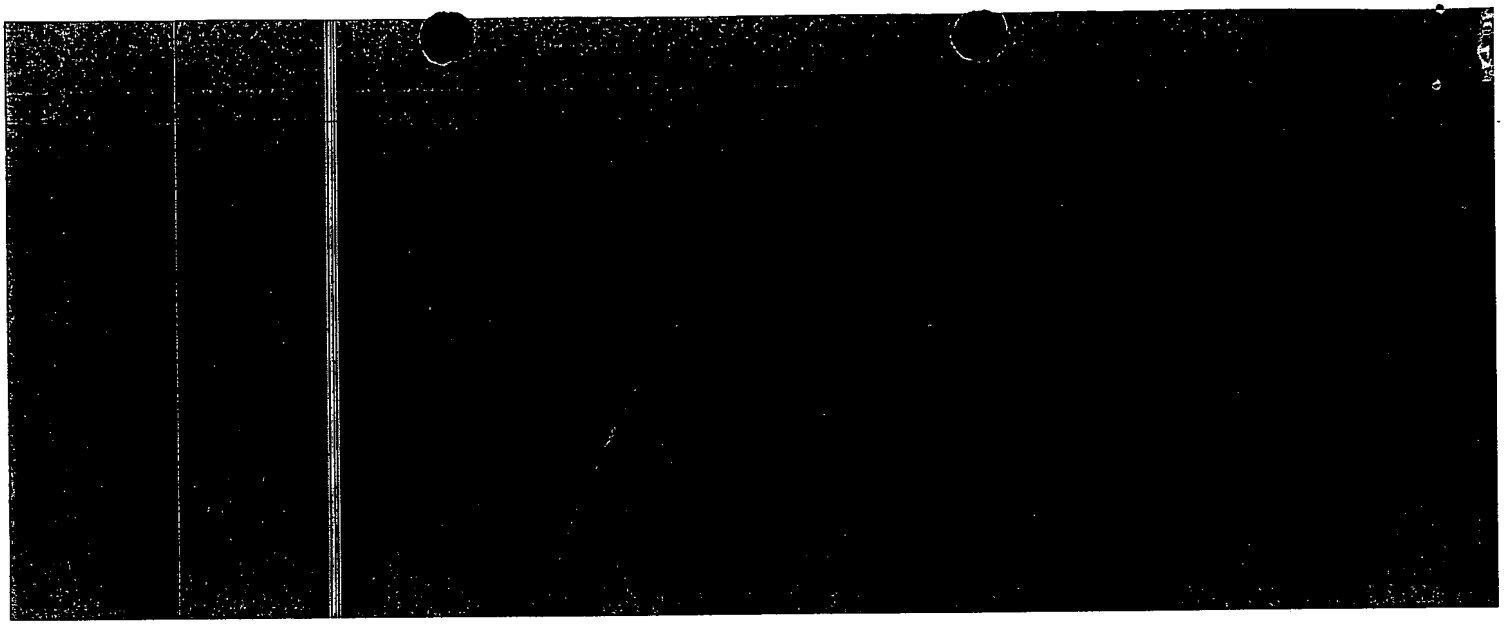
β-lactam antibiotics such as amoxicillin, ampicillin, cephalothin, cefaclor or cefixime; or
macrolides such as erythromycin, or clarithromycin; or
tetracyclines such as tetracycline or doxycycline; or
aminoglycosides such as gentamycin, kanamycin or amikacin; or
quinolones such as norfloxacin, ciprofloxacin or enoxacin; or
others such as metronidazole, nitrofurantoin or chloramphenicol;
or preparations containing bismuth salts such as bismuth subcitrate, bismuth subsalicylate, bismuth subcarbonate, bismuth subnitrate or bismuth subgallate.

56. Novel compounds according to any of claims 20-29 for us in therapy.

57. A process for the preparation of novel compounds of the formula Ia, Ib, Ic Id, Ie or If as defined in any of claims 32-53 by methods known in the art.

58. A process according to claim 57 for the preparation of the novel compounds of formula Ia, Ib, Ic, Id, Ie and If, which process comprises

i) conversion of a monosaccharide to a glycoside with an aglyc n R_a to form the R_a-glycoside derivative in such a way that the R_a-glycoside is possible to transform to a glycosyl donator by activation at the an meric centr ,



SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 94/00604

A. CLASSIFICATION OF SUBJECT MATTER

IPC : C07H 15/04, C07H 15/08, A61K 31/70, A61K 47/48
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC : C07H, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CA, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO, A1, 8604065 (SYNTEK AB), 22 Sept 1994 (22.09.94), see esp. p. 10-11 and p. 38, l. 20-31 --	1-24,27-58
X	DE, A1, 3220427 (BEHRINGWERKE AG), 1 December 1983 (01.12.83), see VIII --	32-58
X	EP, A2, 0069678 (CHOAY S.A), 12 January 1983 (12.01.83), see all examples --	32-58
X	JOURNAL OF CHEMICAL AND ENGINEERING DATA, Vol 9, No. 3, July 1964, Richard G. Schweiger: "Preparation of Alkyl alpha- and beta-L-Fucopyranosides", see page 408-410 --	32-58

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 Sept 1994	07 -10- 1994
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Anna Sjölund Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 94/00604

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE, C2, 2857791 (CHEMBIOMED LTD.), 19 October 1978 (19.10.78), see example 4	32-58
X	GLYCOCONJUGATE J, Volume 3, 1986, Elisabeth Kallin et al, "New Derivatization and Separation Procedures for Reducing Oligosaccharides", page 311 - page 319, see page 312, fig. 1, p. 313, table 1 and page 318	32-58
X	J. REPROD. FERT., Volume 89, 1990, S. Lindenberg et al, "Carbohydrate binding properties of mouse embryos", page 431 - page 439, see table 1	32-58
X	GLYCOCONJUGATE J, Volume 6, 1989, Gérard Strecker et al, "Complete Analysis of the 1H-and 13C-NMR Spectra of Four Blood-group A Active Oligosaccharides", page 271 - page 284, see page 272, figure 1, VII-A-1	32-58
X	STN International, File CA, Chemical Abstracts, volume 118, no. 21, 24 May 1993 (Columbus, Ohio, US), Falk, Per et al: "An in vitro adherence assay reveals that Helicobacter pylori exhibits cell lineage-specific tropism in the human gastric epithelium", Proc. Natl. Acad. Sci. U. S. A., 90(5), 2035-9 (English) 1993	1-24,27-31
A	EP, A2, 0348143 (MARION LABORATORIES, INC.), 27 December 1989 (27.12.89)	1-24,27-31

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were f und unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 25-26
because they relate to subject matter not required to be searched by this Authority, namely:
See PCT Rule 39(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

2. [X] Claims Nos.: 1-24, 27-58
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see next sheet

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite paym nt of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additi nal search fees.

INTERNATIONAL SEARCH REPORT

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The scope of the claims 1-24 and 27-58 is so broadly formulated with a very large number of different glycosides that a meaningful search could not be done. Also, the expression "heterocyclyl" is too broad and lacks differential power. (See Art.6)
It is pointed out that if one or more of the compounds lack novelty, a single general inventive concept will be lacking and the unity of the invention must be questioned.

INTERNATIONAL SEARCH REPORT

27/08/94

International application No.
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